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(54) Title: A DEVICE AND METHOD FOR TEMPORATY OR PERMANENT SUSPENSION OF AN IMPLANTABLE SCAFFOLDING CONTAINING AN ORIFICE FOR PLACEMENT OF A PROSTHETIC OR BIO-PROSTHETIC VALVE

(57) Abstract: In a surgical method for improving cardiac function, an implantable scaffold or valve support device is inserted inside a patient's heart and attached to the heart in a region adjacent to a natural mitral or other heart valve. The scaffold or valve support device defines an orifice and, after the attaching of the scaffold or valve support device to the heart, or temporary support while native valve leaflets and/or subvalvular structures are captured, a prosthetic or bio-prosthetic valve seated in the orifice, and the native valve may be retracted into the scaffold/replacement assembly to create a gasket for sealing the complex.

A DEVICE AND METHOD FOR TEMPORARY OR PERMANENT SUSPENSION OF AN IMPLANTABLE SCAFFOLDING CONTAINING AN ORIFICE FOR PLACEMENT OF A PROSTHETIC OR BIO-PROSTHETIC VALVE

FIELD OF THE INVENTION

The present invention relates to medical devices and procedures, in particular related to the fixation within the heart or blood vessel of a device which enables replacement of a heart valve, and more particularly, to a novel device for use in a novel procedure for performing a catheter-based heart valve replacement.

BACKGROUND OF THE INVENTION

The four valves of the human heart consist of either two or three pliable leaflets attached circumferentially to a fibrous skeletal annulus. Normally, heart valves function to open in one portion of the cardiac cycle, either systole or diastole, (depending on the valve), causing minimal resistance to forward blood flow, but close by hinging from the annulus during the other part of the cardiac cycle, with the leaflets (either two or three) coming into central contact with each other, such that retrograde flow is inhibited.

Heart valve regurgitation, or leakage occurs when the leaflets of the valve fail to come fully into contact. This can be congenital, or the result of a disease process. Regardless of the cause, the leakage interferes with heart function, since it allows the unintended flow of blood back through the valve. Depending on the degree of leakage, the backward flow can become a self-destructive influence on not only function, but also cardiac geometry. Alternatively, abnormal cardiac geometry can cause the leakage, and the two processes are "cooperative" in causing acceleration of abnormal cardiac function.

The result of a valve having significant regurgitation is that a pathological state develops in which blood may be simultaneously pumped both forward through the outflow valve of a chamber and backward through the inflow valve, decreasing forward cardiac output. Depending on the severity of the leakage, the capability and efficiency of the heart to pump adequate blood flow can be compromised. In the case of the two trio-ventricular valves, (the mitral and tricuspid), the process can be caused by myocardial infarction damaging papillary muscles located in the left (or right) ventricle, torn or abnormally elongated chordae tendineae, or in any valve through damaged valve structures by infection, degenerative processes, or stretching of the annulus such that leaflets no longer come into contact by virtue of the increased cross-sectional area. Stretching of the ventricle and increased distance between the papillary muscles can also cause leakage of the atrio-ventricular (A/V) valves.

At present, for the most part, regurgitant valves can be either surgically repaired or replaced, both currently requiring open-heart surgery, use of cardio-pulmonary bypass and stoppage of the heart. Because of the magnitude of the procedure, risk of death, stroke, and

bleeding, respiratory, renal, and other complications is significant enough that many patients are not candidates for treatment. The heart or aorta must be cut open, and even when performed by very experienced surgeons, repairs can fail early, or, if initially successful, are not always durable over time.

In the case of the mitral valve, replacement with a prosthetic or bio-prosthetic valve is associated with a higher operative mortality than repair of the native valve, but does not result in recurrent regurgitation experienced after a repair. The higher mortality is thought to be the result of loss of the function of the papillary muscles of the left ventricle, which are attached to the mitral valve leaflets by cords known as chordae tendineae, which contribute to tethering of the leaflets and systolic shortening of the left ventricle. However, with preservation of these sub-valvular structures, the outcomes equalize, or may be better in severe cases with replacement and sub-valvular structure preservation. (See Ann Thorac Surg 2 81: 1153– 61.)

Even though the prognosis of surgically untreated mitral regurgitation is poor, (see N Engl J Med 2 352:875-83), only 33% of patients with significant regurgitation are referred, due to age, co-morbidities, or physician preference (see European Journal of Cardio-thoracic Surgery 34 (2) 935—936).

In the face of a severe, life threatening pathological process with no treatment offered to a majority of patients due to the magnitude of the risks of currently available therapy, a simpler, less invasive approach to treatment, such as a percutaneous device that can effectively eliminate regurgitation, yet preserve annulo-ventricular in atrio-ventricular connectivity and function, is severely needed.

For this reason, there is widespread development currently underway for placement of valves into the aortic (see Circulation Dec 2002 p. 3006-3008), and Pulmonary, (see J. Am. Coll. Card., vol. 39, May 15, 2002, p. 1664-1669), positions. There are currently a variety of technologies for aortic replacement, but all generally have an expandable support structure for attached pliable leaflets, delivered either through the apex of the ventricle or retrograde through the aorta from the femoral artery (The Journal of Thoracic and Cardiovascular Surgery; October 2008, p 817-819).

Because of the asymmetry of the annuli, as well as the lack of rigidity, the same principals cannot be applied to the mitral and tricuspid valves, or in the aortic valve in the absence of calcification, as in most cases of aortic insufficiency. In the mitral position, several approaches have been pursued. Additionally, in the case of the mitral valve, radial expansion of a prosthetic replacement could impinge on the aortic valve, with which it shares a portion of its annulus along the anterior mitral leaflet.

Primarily, remodeling or alteration (to support or decrease the size) of the mitral annulus by various means has been a focus of intense interest. Some of the most tested of these are those that rely on the perceived anatomic proximity between the posterior annulus

and the coronary sinus (see Webb, et al). Although initially promising, the coronary sinus has been shown in virtually all cases to course on the atrial side of the mitral annular plane, and averages 7 to 11 mm from the annulus, and the distances are variable. Moreover, the distances increase in subjects with mitral regurgitation. (See Choure, et al, J Am. Coll. Card.; Vol. 48, No. 10, 2.) The approach has been largely abandoned.

Another approach is the central apposition of the anterior and posterior leaflets at the midpoint, mimicking the so-called "Alfieri stitch". The benefit comes from creation of central coaptation. Devices to create this reconfiguration have been tested and commercialized, but do not control regurgitation to the degree achieved in replacement.

In general, current heart valve replacement procedures generally require invasive surgery. This, of course, is a long, difficult and complex process and requires that the patient endure significant, invasive surgery. While various alternatives have been proposed to minimize this trauma, there is still a need in the art to further reduce such potential injury.

SUMMARY OF THE INVENTION

Recently a number of prosthetic valve-replacement devices have been developed that can be delivered through a trans-catheter approach, and that expand into the natural annulus of a native valve. Since the mechanism of fixation of these valves is generally radial expansion, either actively or passively, a rigid annulus, (such as with calcification or a previously placed surgical valve or ring), is required, or the replacement valve would distort, or even rupture the heart. In many cases of valve pathology, the disease process does not include a rigid annulus or fibrous skeleton of the heart. Consequently, the benefit of these advances is limited to specific pathological states.

Proof of the concept has been published in the medical literature in a very similar way. Inelastic rings were surgically implanted adjacent to the native mitral valve of sheep. One week later, percutaneous valves were successfully expanded into the rings in all five animals. (See Journal of the American College od Cardiology, Vol. 58, No. 24, 2011.) The current invention enables the implantation of the ring, or neo-annulus, through a catheter.

U.S. Patent Application Publication No. 2010/0262232 and International Patent Application No. PCT/US2010/001077 describe an implantable scaffold that contains a neo-annulus into which a prosthetic or bio-prosthetic valve could be implanted. The present invention seeks to provide a means through which that scaffold, which is rigid, can be inserted such that the radially expanding, trans-catheter valve concept can be extended to valves with pathology not currently amenable to this approach.

In a surgical method for improving cardiac function in accordance with the present invention, an implantable scaffold or valve support device is inserted inside a patient's heart (or blood vessel) and attached in a region adjacent to a natural or native valve. In the heart, the scaffold or valve support may be anchored to the heart wall and/or to the native valve itself. The scaffold or valve support device defines an orifice which receives a prosthetic or

bio-prosthetic valve after disposition of the scaffold or support device in the heart and either before or after anchoring of the scaffold or support to the heart.

A catheter is placed into the appropriate location, and the scaffold assembly is delivered out the tip of the catheter. The scaffold is positioned in part by steering the delivery catheter and in part by manipulating tethers or wires that are removably attached to the scaffold. The wires may be flexible, steerable, or relatively stiff, and may be pre-formed or made of a component with a memory. In one embodiment of the invention, through use of specific fixation methods and devices disclosed herein, the scaffold is then fixed at its margin or body to a heart or blood vessel wall adjacent to a native valve. In sequence, the scaffold is delivered, positioned, and then fixed to the heart or blood vessel wall. With the scaffold or heart valve support system in place, a prosthetic valve can be installed in an annulus or aperture of the scaffold. In an alternative approach described herein, after the scaffold is ejected from the distal end of the delivery catheter into a heart chamber and expanded from a collapsed insertion configuration to an expanded deployment configuration, a prosthetic valve is seated in an orifice of the scaffold and the combined assembly is attached, through use of specific fixation methods and devices disclosed herein, to the leaflets or the subvalvular apparatus of the native valve.

In the case of AV valves, the scaffold or valve support device is at least indirectly secured to chordae tendineae, and therefore, the papillary muscles of the heart. Such a device can distribute forces to the prosthetic valve similar to those typical of the normal, native valve. Thus, the attached or entrained chordae tendineae serve to retain the scaffold and prosthetic valve in position in opposition to systolic blood pressure. The current invention involves in part a method and an associated device for capturing the natural valve and concomitantly and indirectly the subvalvular apparatus and incorporating those structures into the scaffold or heart valve support system, or to the prosthetic valve.

Where the native valve is captured and coupled to a combined scaffold/replacement valve assembly, the scaffold and the replacement valve mounted thereto are attached to the leaflets of a native valve so that the scaffold and the replacement valve are in fluid-sealing engagement with the leaflets. Closure devices may be provided to close commissure gaps, if necessary.

During the implantation procedure, the valve-supporting scaffold may be attached to the heart chamber or vessel wall via at least one but more preferably a plurality of flexible or rigid tensile suspension element(s) or alternatively the scaffold may be held in place by tethers or other supporting elements extending from a delivery or deployment catheter. In either instance, the scaffold or neo-annulus, or the assembly of the combined replacement valve and scaffold or neo-annulus, are attached to the native valve, such that all forces normally borne by the native valve, and to which the replacement valve is now subjected, are transmitted to the native valve, and its subvalvular apparatus, in the case of atrio-

ventricular valves.

A scaffold or neo-annulus in accordance with the present invention, if employed in a setting wherein attachment of the valve directly into the annulus of a native heart valve is not ideal, possible, or otherwise feasible, enables valve placement wherein it otherwise could not occur, yet maintains the normal transmission of forces from the replacement valve to the native valve. The present invention provides devices and mechanisms for fixation of the suspension elements to the heart or vessel wall, as well as devices and mechanisms for incorporation of the sub-valvular apparatus, in the case of atrio-ventricular valves, (or to the native valve in the case of ventricular outflow valves), to the implanted scaffold or neo-annulus.

Fixation of Neo-annulus Suspension Elements to Heart or Blood Vessel Wall

Deployment of a replacement valve through a trans-catheter approach requires first that there is a stable, inelastic valve support scaffold with an orifice into which the replacement valve can be inserted. Stability can be achieved through fixation of such a valve support scaffold to the heart or blood vessel wall. In this embodiment, the process requires first that the scaffold or valve support device be suspended or supported. This scaffold-like element defines, in one embodiment, of an orifice into which the valve will ultimately be deployed, which is suspended by one or a plurality of structural elements of the device, which fixes it to a heart or blood vessel wall.

Therefore, the neo-annulus scaffold may be actively suspended from the heart or blood vessel wall through the use of one or more suspension elements, each an elongate flexible tensile element. The suspension element(s) may be actively or automatically affixed to the heart or blood vessel wall. In the case of active attachment, the suspension element(s) may each be provided with a deployment tether that extends through the deployment catheter to a site of proposed fixation on the suspension element to the heart or blood vessel wall (for example, the end of suspension component remote from its attachment the neo-annulus). With the neo-annulus supported in its desired location, the end of the suspension element is advanced to the proposed site of fixation on the heart or blood vessel wall, and a helical or alternatively-shaped, screw-type fixation or similar component or a pronged staple or other fixation element is used to secure the suspension element to the heart or blood vessel wall.

Once the appropriate locus for fixation of the suspension component(s) on the heart or blood vessel wall has been reached, the tethers used to deliver fixation device(s) to the suspension element(s) may be used both to create fixation and to manipulate/position the suspension element(s). By advancement of the fixation device(s) over the tether(s), a means is provided whereby manipulation of fixation elements and placement of the elements in a specific location in the heart or blood vessel wall. Fixation of the suspension element(s), once achieved, provides support for the neo-annulus, because of its connection to the heart

or blood vessel wall by (an) intervening member(s), which is (are) the suspension element(s).

The attachment, or fixation, of a suspension element to the heart or blood vessel wall may be made by a separate component, such as a staple, clip or device of other appropriate design delivered by a separate component, or may be an integral part of the suspension element itself, such as a burr, barb, hook, or other appropriate fixation element. In general, the suspension elements are likely to be sigmoid or somewhat linear structures, extending radially from the orifice-defining neo-annulus scaffold to the point of attachment to the heart or blood vessel wall.

The suspension element or elements are generally part of the construction of, or attached to, the scaffold or neo-annulus as a whole, and are attached or otherwise fixed to the scaffold, extending to the heart or blood vessel wall, wherein the suspension element(s) are attached. However, the suspension elements may be separate structures and be delivered and attached to the neo-annulus in-situ. The suspension elements may be of any length, so that the neo-annulus may be somewhat distant, very near, of even essentially in contact with the wall adjacent to the valve or annulus.

In one embodiment, the orifice-defining neo-annulus scaffold preferably takes the form of a ring. The ring made be made of nitinol or other shape-memory material with a temperature induced memory or other means by which the scaffold assumes a substantially rigid, or at least inelastic configuration of pre-determined shape after ejection from the delivery or deployment catheter. Alternatively, it may be passively expanded and be made of another appropriate material, such as a weave, fabric, or monofilament material. The scaffold is optionally provided with the above-described linear suspension components, which are extendible outwardly to attach to the heart or blood vessel wall near the native valve for which replacement is intended. The suspension elements may be of any length or shape, and may appear like spider legs, or as ring-topped, flattened tripod (in in instance wherein three such elements are used). They are constructed preferably of a spring-like material and are curved to allow for fixation to a heart or blood vessel wall of variable contour, as well as for excursion of the neo-annulus toward or away from the valve as necessary, but may be in any appropriate configuration.

The suspension components or "legs" are, in an especially preferred embodiment, permanently attached/constructed to the valve-support ring, but are of a material and design that allows them to assume a folded or collapsed configuration within the delivery catheter. The suspension elements may be actively extended by deployment tethers operated from outside the subject or automatically extended, in the case of a spring-like material, when released. Also, the suspension elements may either be actively guided toward, or designed in a way as to extend automatically to, the heart or blood vessel wall, wherein fixation of the ends of the suspension elements to the heart or blood vessel wall will ensue. Alternatively

they may be actively deployed, as by balloon expansion or other method.

In the passive-fixation iteration of the device, each of the one or more suspension elements has a barb, hook or other appropriate fixation element at its free end. Apposition of the hook, barb, or other appropriate fixation element to the heart or blood vessel wall results in attachment of the respective suspension element to the heart or blood vessel wall. This automatic attachment may be by an expansion or piercing or other passive fixation element. The suspension elements are each configured to passively connected to the heart or blood vessel wall. In the most preferred iteration, the hook, barb, burr, or other appropriate component is manipulated by a tether or other similar component of the suspension capable of the manipulation/engagement, but amenable to subsequent removal. This could occur through release of a self-expansile suspension element that engages and attaches to the heart or blood vessel wall as it expands, as in the case of an expanding metal or other memory-like material that expands when released and pierces the heart or blood vessel wall.

With the neo-annulus located adjacent to the native valve, allowing free flow through its center, and fixation to the heart or blood vessel wall adjacent to the native heart valve, the valve replacement process requires deployment of the valve, and simultaneous or subsequent capture of the native valve and fixation to the neo-annulus/replacement valve complex. In both iterations, the valve-capture tension elements are incorporated into the neo-annulus so as to transmit forces generated by cardiac function to the neo-annulus, and the tethers run over or near the tension elements to allow a "push-pull" on the neo-annulus relative to the native valve.

The orifice, which is more or less central to the device, is generally circular or becomes generally circular, and is defined by an inelastic scaffold or neo-annulus into which a replacement valve can be deployed, the scaffold or neo-annulus being deliverable through a delivery catheter placed at an appropriate position in a heart chamber or blood vessel through a percutaneous, trans-vascular approach.

Therefore, the valve-supporting scaffold is flexible and capable of being collapsed, folded, twisted, or otherwise compressed that it can assume a low profile for delivery but becomes a generally round or otherwise appropriate configuration after delivery. The scaffold or neo-annulus may be reconfigured passively or automatically, for example, by being made of a temperature-sensitive or non-temperature sensitive shape memory material that reconstitutes when liberated from a compressed or folded state. Alternatively, reformation into an appropriately round shape may be active, such as by placement of a central expansile element, such as an inflatable balloon, that actively creates a round orifice or central neo-annulus before deployment of a replacement valve.

In one embodiment, the orifice-defining neo-annulus scaffold preferably takes the form of a ring. The ring made be made of nitinol with a temperature induced memory by

which the scaffold, having been delivered in a flexible configuration, assumes a substantially rigid configuration of pre-determined shape after ejection from the delivery or deployment catheter. The scaffold is optionally provided with the above-described linear suspension components, which are extendible radially, or generally in an outward direction, to attach to the heart or blood vessel wall near the native valve for which replacement is intended. The suspension elements appear like spider legs, or as ring-topped, flattened tripod (in in instance wherein three such elements are used), or other appropriate configuration. They are constructed preferably of a spring-like material and are curved to allow for fixation to a heart or blood vessel wall of variable contour, and allow for excursion of the neo-annulus toward or away from the valve as necessary.

Since most replacement valves are deployed by radial expansion, the orifice or neo-annulus is preferably flexible for at least a given time after ejection from the delivery catheter, so as to allow manipulation and reconfiguration after delivery, but also relatively inelastic so that a radially expanded valve does not distort it. The valve-supporting scaffold or neo-annulus may therefore be constructed of a braided or monofilament metal or other appropriate synthetic or naturally occurring material with the appropriate physical characteristics.

The scaffold or heart valve support device is thus delivered through a catheter in a collapsed configuration, and so is compressible or otherwise reconfigurable to fit into the lumen of a delivery catheter. After delivery through the tip of a delivery catheter, the scaffold device is be suspended and fixed in a position adjacent to a heart valve for which replacement is considered, and into which a valve can subsequently be placed.

Suspension element(s), as well as the neo-annulus, may be covered or coated with a substance to enhance tissue ingrowth, prevent clot or blood adhesion, may be drug eluting, have heparin or other substance bonding, or or otherwise be constructed of a material that enhances tissue ingrowth, prevent clot or blood adhesion, or other properties deemed to be advantageous.

After suspension by the elements, attachment to the native valve leaflets and replacement valve deployment follow essentially as disclosed hereafter.

Stabilization of Neo-annulus Through Temporary Support Through Delivery Catheter Prior to Capture of Native Vale/Subvalvular Apparatus, Without Fixation to Heart or Blood Vessel Wall

Deployment of a replacement valve through a trans-catheter approach requires first that there is a stable, rigid or inelastic neo-annulus, or orifice, into which the replacement valve can be inserted. Stability can be achieved through temporary support of the neo-annulus or orifice without permanent fixation to the heart or blood vessel wall.

In this approach, the valve-receiving scaffold is suspended through or by the delivery system while the valve is deployed and the native valve leaflets are incorporated into the

neo-annulus or replacement valve. Thereafter, since fixation of the neo-annulus and replacement valve deployed therein to the native heart valve or subvalvular apparatus is completely supportive of the implanted devices, the connection to and support from the delivery system may be interrupted and the replacement-valve/neo-annulus left in situ, with forces on the replacement valve being transferred to the native valve (and the subvalvular apparatus, in the case of A/V valves), wherein they are borne in the normal or natural physiological state.

In this embodiment, the neo-annulus may be suspended by a single tether or a plurality of tethers (preferably three or four) that allow both support and positional maneuvering of the neo-annulus. The tethers are removable when the need for support no longer exists. Thus the neo-annulus is deployed via the delivery system connected to the tethers, and after either actively or passively expanding, is positioned and supported over the orifice of the targeted native valve. Most preferably, the tethers are placed over or near tensile coupling elements having free or distal ends adapted to entrain, capture, and grasp native valve leaflets. The tethers are slidable relative to the tension/tensile coupling elements and engage the neo-annulus or scaffold so as to enable the operator to push the scaffold in a distal direction while holding or pulling on the tensile coupling elements, thereby approximating the scaffold (typically with replacement valve mounted thereto) and the leaflets of the native valve.

Regardless of the support/suspension strategy (suspension elements or temporary support through the delivery system), the suspended neo-annulus is supported at least in part by the positioning tethers that pass over the tensile coupling elements. The tensile coupling elements pass through or otherwise are incorporated into the substance of the neo-annulus. On the distal ends of the tension elements are devices for capturing and entraining the native valve leaflets, to retract the native valve leaflets and bring them into contact or near contact with the neo-annulus.

The devices for valve leaflet capture are hooks (e.g., grappling hooks), barbs, clips, burrs, or other appropriate entrainment components that allow adherence/fixation of the tension elements to the valve leaflets while still allowing their normal or near normal excursion. Thus, until engaged, valve leaflets have continued "normal" (or with no or minimal additional impediment), or near normal function until such time as they are captured and tethered/incorporated into the neo-annulus/replacement valve complex by simultaneous "forward" or distally (in the direction of forward blood flow) directed force on the tethers and retracting force on the tension elements within or near the tethers.

The hooks, barbs, clips, burrs, or other appropriate components may penetrate, impinge, entrap, clip over, or in any other appropriate way engage the leaflet so as to allow tension to be placed permanently thereon by traction elements to which the hooks, barbs, burrs, or other appropriate components are attached. Since the tension elements are

incorporated into an aspect of the neo-annulus or central orifice, the valve leaflets may be pulled into contact with the neo-annulus or central orifice.

To create the excursion of the neo-annulus with its orifice toward the native valve leaflets in a preferred embodiment, the tension members are retracted or pulled in a proximal direction from the proximal end (i.e., outside of the body) as the tethers, generally tubular members surrounding portions of the tension members, are advanced in a distal direction from the proximal end of the delivery catheter. The opposing forces cause the valve-supporting neo-annulus or scaffold with its valve-receiving orifice to move toward the native valve. In general, since this excursion may also disrupt native valvular function, it is contemplated that the replacement valve will have been deployed into the central orifice of the neo-annulus or scaffold before the final approximation excursion is generated.

It is possible for the neo-annulus to be delivered through a catheter passed directly through the heart wall. In the case of the A/V valves, entry may be made through a ventricle and the neo-annulus suspended proximal to the valve on the atrial side. In that approach, the support of the valve or sub-valvular structures is achieved from the ventricular side, reversing the above-discussed neo-annulus seating and supporting procedure. More specifically, in order to approximate a valve support member or scaffold and the leaflets of a native valve to one another in a trans-ventricle procedure, the scaffold or valve support member may be pulled in the proximal direction (towards to operating surgeon) while the valve leaflets are held or pushed in the distal direction. In another event, appropriate forces are exerted in order to mover the scaffold or valve support member on the one hand and the valve leaflets on the other hand towards one another and into force-transmitting and effective fluid-sealing contact.

To permanently position the replacement-valve/scaffold complex in a fluid-sealing engagement with the valve leaflets, the tension or tensile coupling elements preferably have a "lock" such as a one-way incremental movement device in the nature of a ratchet. The ratchet may take the form of cooperating tooth formations and a tapered passageway or spring loaded latch, a cam, a compression device or other appropriate component that prevents the valve-supporting neo-annulus or scaffold member from moving away from the native valve, once having moved toward it. The lock may be built into the neo-annulus or scaffold, or be a separate component, advanced over the tension element toward the neo-annulus or central orifice.

Once the neo-annulus/replacement valve complex has become fixed to the native valve, creating a seal, the neo-annulus is supported by the native valve leaflets. The neo-annulus or scaffold may be additionally supported by tensile suspension elements attached to the cardio-vascular wall, particularly in the event that such suspension elements are used to hold the neo-annulus or scaffold in place during the implantation procedure.

After the securing of the neo-annulus or scaffold to the native valve leaflets,

positioning tethers can be removed, as well as proximal portions of the tensile coupling elements, The distal end portions of the tensile coupling elements remain in place holding the neo-annulus to the native valve leaflets in tension, the final position of the neo-annulus or scaffold being secured through the "lock" mechanism.

It is possible that after restriction/capture of the valve leaflets, the neo-annulus/captured valve contact will not completely eliminate leakage around the valve. In one embodiment of an implantation system in accordance with the invention, an inflatable or otherwise expandable component such as an annular bladder can be enlarged around the neo-annulus to further inhibit paravalvular leak and enhance the seal between the native valve and the scaffold/replacement valve. This sealing component may initially take the form of a collapsed inner-tube-like component that is attached to the neo-annulus or that is separately delivered and positioned in situ. The inflatable sealing component is provided with an inflation tube through which air, saline solution, another fluid, or other appropriate substance, such as polymers, is infused, expanding the sealing component to eliminate potential or actual peri-valvular leak. After expansion of the sealing component, the inflation tube is removed /plugged, or otherwise eliminated from permanent connection with the inflatable sealing component. Also, a fluid, such as saline, may be initially infused, but later be exchanged for another, potentially permanent material, such as a polymer or orher material of appropriate properties.

In addition to acting as a means of resolving perivalvular leakage, the circumferential or partially circumferential inflatable component may be used simply as a means to make the apposition of native valve and neo-annulus less erosive, less distorting to the heart, more likely to fit a rigid neo-annulus/replacement valve complex into a generally soft, beating heart without long-term tissue change, or other potentially desirable characteristics. In essence, the inflatable component may impart the characteristics of a "sewing ring" such as is found on most valves constructed for open surgical implantation.

The inflatable sealing component may be delivered as a separate element, or be a part of the construct of the central orifice or neo-annulus. It may be constructed of an elastic material or one of fixed volume and/or shape, regardless of the pressure of its internal contents. It may be filled with fluid long-term, or have a permanent polymer that can be infused primarily, or as a replacement for an initial fluid or gas infusate. It may be covered or coated with a substance to enhance tissue ingrowth, prevent clot or blood adhesion, may be drug eluting, heparin or other substance bonding, or otherwise be constructed of a material that enhances tissue ingrowth, prevent clot or blood adhesion

Alternatively, an implantable clip, barb, staple or other approximation device of appropriate design may be placed at the site of a gap between native valve leaflets for bringing the leaflets into apposition around the scaffold or valve support device to obliterate a site of perivalvular leakage. One such device for perforating two nearby tissue strictures

has a multi-pronged or multiply legged "V", "U", "Y" structure or other similarly shaped component, such that after perforation of the generally two, or paired, barbs on the clip into the tissue structures, advancing the clip in one direction (in the examples described, upward) the perforation sites are brought into apposition.

Such a clip-like approximation device is constructed of a metallic or other appropriate material, may have memory, and are placed and manipulated through the delivery system or other means. It is affixed in place, as with bending the arms outward, automatically springing when released, fixation with a separate element, or other appropriate means. Alternatively, a spring-like device, suture-like device, staple-like device, or other means of apposing native valve leaflets at gaps may be used.

The leaflet approximation device may be introduced prior to introduction of the remainder of the implantable devices, creating a smaller orifice in the native valve, and enabling a potentially more complete circumferentially solid line of contact between the neo-annulus/replacement valve complex. Therefore the capture of the native valve, introduction of the scaffold, deployment of the replacement valve may follow apposition of the commissures, in order to diminish the size of the native vale orifice.

In general, in the implantation embodiment wherein the neo-annulus is only temporarily supported by the delivery system while permanent fixation to the native valve is achieved (or if suspended by either elongate elements, as disclosed above, or by a membranous component disclosed previously, and after suspension has been accomplished), the placement of the scaffold and replacement valve may consist of a procedure summarized as follows:

- A delivery system is inserted through the vascular system or heart wall to an appropriate site in a heart chamber or blood vessel near a valve to be replaced.
- A device consisting of the tensile coupling elements for valve capture, the neo-annulus, suspension elements, if appropriate, support tethers, and other components, as required, is advanced out of the delivery system.
- The valve leaflets are engaged by the tensile coupling elements incorporated into or attached to the neo-annulus. In some iterations, where a heart wall is used for introduction, these tensile elements may be compressive.
- The neo-annulus is suspended to the heart or blood vessel wall if appropriate, or alternatively, supported only by tethers emanating from the delivery system.
- The replacement valve is deployed into the neo-annulus.
- The native valve is retracted by the tensile coupling elements with entrainment or capture components on their ends, such that the retracted leaflets form a "gasket"-like element toward or around the perimeter of the

replacement valve/neo-annulus complex, eliminating leak and retracting the native valve out of the inflow or outflow tract to or from the native valve. Separate or incorporated locking devices integrated with the tension elements cause a "one-way" tightening of the tension elements, so that the leaflets are retracted into the neo-annulus/replacement valve complex.

- The inflatable element, if used, is inflated to eliminate peri-valvular leakage. The initial inflation substance can then be replaced if appropriate, and imaging confirms elimination of peri-valvular leak. Alternatively, a hook, barb, clip, or other device of appropriate design is placed into adjacent native valve leaflets at the site of a gap, such that valve leaflets are apposed.
- Tethers, tubes, extensions of tension elements are finally removed, leaving only the replacement valve, neo-annulus, and inflatable component or gap-closure device, if used. Any other appendages associated with delivery, deployment, stabilization, fixation, valve capture, inflation, etc. are removed.
- As an alternative, the commissures may be apposed prior to the implementation of the above sequence.

Capture of the native valve

With certain valves in the heart, specifically the atrio-ventricular valves, the sub-valvular structures are important for chamber function. It has been recommended, therefore, when replacement is performed rather than repair, that these structures be incorporated into the annulus of the new valve. (See M. A. Borger, et al Ann Thoracic Surg 2006; 81:1153-1161.) The current invention provides a device and method for incorporation of these structures into the scaffolding, thereby preserving ventriculo-annular contribution to systolic function.

Accordingly, the current invention also contemplates a device and means for attachment of the native valve, or sub-valvular structures (in the case of the mitral or tricuspid valves) to either the neo-annulus or another part of the implanted scaffold. In the principal embodiment, attachment elements consist of single or multiple hooks, single or multiple barbs, or other appropriate means of grasping the valve leaflet(s) or chordae tendineae, and attaching them either directly or with an intervening element to some portion of the scaffold, such that, in the case of the atrio-ventricular (A/V) valves, systolic ventricular forces on a valve implanted into the neo-annulus will be transmitted to the papillary muscles and cords rather than to the fixation points of the scaffold margin alone, thus preserving systolic A/V valvular/papillary function.

In a particularly preferred embodiment, the valve leaflets are "snagged" by one or more hooks or barbs. As discussed above, a device with multiple hooks is incorporated, through tensile or compressive coupling members, into the neo-annulus, and is delivered through the native valve orifice during the entrainment process by bringing the neo-annulus

toward the leaflets or subvalvular structures. The hooked device may be advanced through a catheter and across the native valve orifice prior to emergence through the delivery system of the neo-annulus and suspension elements, if used, or advanced from the ventricle, in the case where a transmural (across a heart wall) approach is used. In other words, the valve capture elements may be first out of the delivery system, followed by the neo-annulus, followed by the suspension elements, if used, or the last, depending on the direction of deployment and delivery. In this way, minimal delivery system size may be possible. Other sequences of delivery are possible.

The hooks, barbs, clips, or other appropriate components attached to the tensile coupling elements may precede the delivery of the remainder of the scaffold out of the delivery catheter. The hooks, barbs, clips, or other appropriate components may have one or more separate delivery components, which enable the capture of the leaflets. The hooks, barbs, clips, or other appropriate components are removably or temporarily attached to the delivery or deployment device, which may advance the hooks or barbs out of the catheter and into the valve orifice as noted above. In a preferred approach, the hooks may "snap" into a delivery element, or may be freely advanced through a native valve, and are passed from a delivery catheter through the valve orifice, between leaflets. The delivery element may have the capability of manipulating the location on the native valve wherein the hooks, barbs, clips, or other appropriate components are engaged to the native valve.

Alternatively, the delivery catheter may cross the native valve, deliver the hooks, barbs, burrs, or other valve capture elements, then retract back across the native valve before releasing the neo-annulus and other components.

The deployment elements may then orient the hooks or barbs, and subsequently release them once the leaflets were engaged by the hooks or barbs. The tensile coupling elements on the hooks may be used to further manipulate the hooks or barbs, such as twisting or applying tension to increase or maintain purchase of the hook or barb on the leaflet.

In a preferred embodiment, tension or tensile members attached to the hooks or barbs used to capture the valve leaflets may be permanently attached to or through a retention element of the scaffold or neo-annulus, generally at outer edge, so as to facilitate the apposition of the native valve around the edge of the neo-annulus/replacement valve complex. Alternatively, the elements may be secondarily attached to the neo-annulus or scaffold.

Because the coaptation surface of some valves is linear, while the replacement or prosthetic valve to be placed is round, it may be desirable to have the hooks or barbs dispersed or spread around the perimeter of the neo-annulus/replacement valve complex. In the most preferred embodiment, the tension/tensile members are preferably distributed at intervals around the neo-annulus. Alternatively, they may be spread separately after exiting

from their connection to the central orifice on neo-annulus.

Therefore, there may be a feature of the deployment element that fans out or separates the hooks or barbs as they leave the delivery catheter. Such a device element may consist of a released spring, elastic material, pre-shaped memory substances, active opening, or other appropriate means of dispersing or separating the hooks or barbs over a length of valve leaflet before attachment of the valve-grasping element to the scaffold or valve support system.

In order to assist in the delivery of the valve-capture elements, which are hooks, barbs, or other appropriate elements designed to engage the native valve leaflets, the hooks, barbs, or other appropriate elements may be collapsed or otherwise constrained into a lower profile configuration. This enhances delivery and minimizes native-valve functional disruption prior to fixation to the native valve, replacement valve deployment, and native valve capture. As such, the hooks, clips, barbs, or other appropriate elements may be actively configured into a low profile, as when bound by a fabric or other constraint element, which is removed or otherwise released prior to engagement with the valve leaflets. Alternatively, the hooks, barbs, or other appropriate elements may be formed of a self-expanding material, such that the intended profile/configuration may be taken on after delivery.

Tethers, tension elements, infusion ports, or other appendages, if fixed to the implantable devices, may be severed or otherwise separated from the implantable devices through the use of an end-cutting device, which can be individually passed over or near the appendage. Alternatively, an attenuated area may be constructed into the appendage such that a natural breakage site can create a severance by twisting, pulling or otherwise manipulating the appendage. Other means of separating tethers, tension elements, infusion ports, or other appendages, if fixed to the implantable devices, as appropriate, may be employed, either through the characteristics of the ancillary elements or appendages, or through introduction of a separate component to create the separation, as appropriate.

The present invention allows attachment of the central orifice or neo-annulus to the heart or blood vessel wall by a continuous suspension element (previously disclosed, see U.S. Patent Application Publication No. 2010/0262232 and International Patent Application No. PCT/US2010/001077), by discontinuous suspension components, with or without a specific margin. Alternatively, the central orifice or neo-annulus may be supported only by the delivery system until fixation of the orifice ore neo-annulus to the native valve can be achieved.

In the current disclosure, the scaffold can be secured to the heart or vessel wall, such that a valve may be delivered through a limited intrusion by utilizing a catheter to deliver and assemble the heart valve components in-situ. This disclosure describes a scaffold which may be attached to the heart or blood vessel wall in a limited way, or else simply stabilized

while the valve is inserted, deployed, and subsequently affixed to the native valve, rendering the initial attachment of the scaffold, or neo-annulus of lesser or only temporary importance to the ultimate fixation of the replacement valve.

Because the replacement valve must be deployed into approximately the same location as the native valve, it is necessary to alter the position of the native valve. In the current invention, a mechanism for pulling the native valve leaflets toward the periphery of the neo-annulus and away from the valve center is also provided

Because this fixation of the generally round scaffold, or neo-annulus to the native valve would require that the two be more-or-less sealed circumferentially, it is possible that native valve leaflets may require plication or otherwise reconfiguration, such that peri-valvular leakage does not occur. A device and method for achieving this reconfiguration is disclosed herein.

Attachment of scaffold to heart wall via fasteners slid along respective tethers

The present invention provides devices and mechanisms for fixation of a margin of a scaffold or vavle support device to the heart or vessel wall, as well as devices and mechanisms for incorporation of the sub-valvular apparatus, in the case of atrio-ventricular valves, to the implanted scaffold or neo-annulus..

In the principal embodiment of the present invention, the scaffold has a series of tethers or support elements attached to its outer edge or margin at intervals around its circumference. In this iteration, there are preferably primary and secondary tethers. The margin of the scaffold or valve support is attached to the heart or vessel wall at the points on the margin where the primary tethers are attached. Because three points determine a plane, in most cases there are three primary tethers (but could be more or fewer). Secondary tethers may be used to position additional fixation points of the scaffold margin after the scaffold margin is attached to the implantation site at the primary points. In some cases it may not be necessary for the secondary tethers to have the ability to manipulate the margin of the scaffold.

The scaffold, which is generally delivered through the lumen of a catheter, is advanced out the tip of said delivery catheter and manipulated in into the desired position through the process of advancing or retracting the primary tethers. The delivery catheter is advanced through the blood vessels or cardiac chamber of the patient and positioned in the appropriate site for scaffold delivery and subsequent fixation. In general, the scaffold is crimped or otherwise packed in the catheter lumen, then pushed or otherwise extruded from said catheter. The scaffold may expand automatically from the collapsed insertion configuration to the opened implantation configuration.

In a preferred embodiment, the tip of the delivery catheter is steerable in at least one direction, such that the position of the scaffold can be directed to the proper location, not unlike a movie projector aims a film image at a screen. The steering element may be a

property of the delivery catheter on by placing a movable element into the catheter lumen after the scaffold has been advanced. The scaffold can be moved toward the appropriate location by advancing or otherwise manipulating the tethers. The orientation of the scaffold is controlled by differentially advancing the tethers, particularly the primary tethers. Steerability may not be needed in instances where a heart wall is the site of introduction of the delivery system.

Once the appropriate locus of the scaffold margin has been reached, the tethers serve not only as holders to maintain position of the scaffold position, but also as support for passage and placement of margin fixation devices. In this embodiment, the sites and number of fixation points are determinable by the number and spacing of the primary and secondary tethers around the scaffold margin.

Once fixation is deemed to be satisfactory, and fasteners have been advanced or otherwise placed, the tethers are detached from the scaffold margin, leaving the scaffold, attached at intervals around its circumference, to the heart or blood vessel wall. By advancement of the fixation devices over the tethers, a means is provided whereby manipulation of fixation elements and placement of those elements at specific points around the circumference of the scaffold from a remote location and through a catheter is possible. Fixation of the outer scaffold margin to the heart, once achieved, provides support for the neo-annulus, because of its connection to the margin by an intervening member such as a membrane.

In a principal iteration, fixation elements slide over the primary and secondary tethers, advanced by sheaths slidably positioned around and over the tethers. The fixation elements, in one form, consist of individual screw-like devices, each of which is located on a respective one of the tethers. The devices in this case each comprise a double helix attached to a cap that may take the form or a circular disk. The cap has a hole and is passed over the tether (the tether traversing the hole), such that the screw-like fixation device can be advanced over the respective tether to the margin of the scaffold and into the heart or vessel wall.

The double helix can be either twisted or simply pressed into the wall. Typically, pushing the associated sheath in the distal direction over the respective tether and against the cap of the screw-like fastener or fixation device first causes the distal tips of the helix wires to insert into the tissue and then induces turning of the helix about its longitudinal axis. The helices may have one or more barbs or other elements to inhibit their unintended dislocation. Such a barb or other element may be activated after acceptable deployment has been achieved. Once the fixation element is embedded in the heart or blood vessel wall, the tether can be detached (for instance, by a twisting action or a simple withdrawal), leaving the fixation element holding the scaffold margin to the wall. In this instance, the cap can straddle the margin with one or both of the helical elements perforating the membranous

element.

Alternatively, the fixation elements or fasteners may take the form of a double, pronged or pincer-like staple or other appropriate design, pre-formed or super-elastic element that, when applied to the margin over the tether, fixates the margin to the heart or vessel wall. There may be an element of the device in this instance to hold the margin element with or without perforating the membranous element of the scaffold.

In any fastener or staple design, there may an element in the cap of the fastener or staple that prohibits the dislodgement of that fastener. For example, the cap of a helical fixation element may have a pin, which when advanced, enters the heart or blood vessel wall and prohibits unintentional untwisting and removal. Similarly, staples or pronged fasteners may have a spring-loaded barb or hook, which advances into the heart or blood vessel wall with no resistance but prohibits withdrawal of the staple.

The tethers may be disconnected from the scaffold after fixation either by unscrewing, twisting to fracture, or other means of separation from the margin of the scaffold. Alternatively, a tool can be introduced into the target heart or blood vessel that is manipulated to induce the separation.

With certain valves in the heart (specifically the atrio-ventricular valves), the sub-valvular structures are important for chamber function. It has been recommended, therefore, when replacement is performed rather than repair, that these structures be incorporated into the annulus of the new valve. (See M. A. Borger, et al Ann Thoracic Surg 2 81:1153-1161.) The present invention provides a device and method for incorporation of these structures into the scaffolding, thereby preserving ventriculo-annular contribution to systolic function.

Accordingly, another feature of the present invention relates to a device and means for attachment of the native valve, or sub-valvular structures (in the case of the mitral or tricuspid valves) to either the neo-annulus or another part of the implanted scaffold. In the principal embodiment, these consist of one or more hooks, clips, barbs, or other appropriate means of grasping the valve leaflet(s) or cordae tendineae and attaching them either directly or with an intervening element to some portion of the scaffold, such that, in the case of the atrio-ventricular (A/V) valves, systolic ventricular forces on a valve implanted into the neo-annulus will be transmitted to the papillary muscles and cords rather than to the fixation points of the scaffold margin alone, thus preserving systolic A/V valvular/papillary function.

In a preferred embodiment, the incorporation of the valve or sub-valvular elements is accomplished after the scaffold or valve-support device has been fixed to the heart or blood vessel wall. A separate tool is then introduced into the chamber or blood vessel whereby the valve leaflets are "snagged" by one or more hooks or barbs. In a most preferred embodiment, a device with multiple hooks is advanced through a catheter and across the valve orifice when it opened, as in forward flow, and retracted when the valve closes, piercing or otherwise capturing the leaflets, such that they (the leaflets) can be pulled into

the scaffold as desired. In such an embodiment, the hooks or barbs separate so that the individual leaflets are not tethered to each other when the cycle requires the valve to open, thereby avoiding an obstruction.

The hooks or barbs, which actually capture or entrain the leaflets, may be reversibly or temporarily attached to a delivery or deployment device, which advances the hooks or barbs out of a catheter and through the valve orifice as noted above. In one iteration, the hooks attach or snap into a deployment element, which is passed from a delivery catheter through the valve orifice, between the leaflets. The delivery or deployment device then orients the hooks or barbs, and either actively or passively releases them once the hooks or barbs engage the leaflets. Tethers (tensile elements) may be attached to the hooks or barbs for use in further manipulating the hooks or barbs, such as by twisting or applying tension to increase or maintain purchase of the hooks or barbs into the leaflets or subvalvular structure.

Because the coaptation surface of some valves is linear or planer, while the replacement or prosthetic valve to be placed is round, it may be desirable to have the hooks or barbs dispersed or spread around the perimeter of the replacement valve. Therefore, there may be a feature of the deployment element that "fans out" or separates the hooks or barbs as they leave the delivery catheter. Such a device element could consist of a released spring, elastic material, pre-shaped memory substances, active opening, or other appropriate means of dispersing or separating the hooks or barbs over a length of valve leaflet before attachment of the valve-grasping elements to the scaffold or valve support system.

The present invention contemplates snagging the valve leaflets and rolling them up into the new valve annulus or into the scaffold or valve support system. The natural valve leaflets are generally disabled by being marginalized, around the edge of the new valve or neo-annular element of the scaffold or heart valve support system. This procedure is akin to gathering a curtain at the edge of a window and wrapping it tight to the new frame. In the case of the A/V valves, the cordae tendenae, which are still attached to the papillary muscles or ventricular wall, transmit their forces to the margin of the new valve or the scaffold. The force generated by ventricular systole keeps the prosthetic valve and scaffold from being dislodged into the atrium.

Another issue is that the anterior leaflet of the mitral valve, if malpositioned, can obstruct the LV outflow tract causing subvalvular aortic stenosis. This is called "SAM", or systolic anterior motion, and can be the consequence of mitral repair done imperfectly. With a pure in-valve replacement of the mitral, the anterior leaflet may be displaced into the sub-aortic position, which would potentially create SAM and could be deleterious to cardiac function.

The present invention contemplates a leaflet capture device with hooks, barbs, or other appropriate components that grasp and entrain the valve leaflet edges and curl the

leaflets against the replacement valve annulus or scaffold margin, thereby retracting and disabling the leaflets around the margin of the replacement valve or into the scaffold. This procedure has the additional benefit of sealing the edge or margin of the scaffold against leakage. The bunched up leaflets serve as a "gasket" against leakage of blood back into the atrium, thereby making discontinuous attachment to the heart or blood vessel wall of the scaffold margin to the atrial wall feasible from a standpoint of valvular or peri-valvular regurgitation.

In the case of the aortic or pulmonary valves, the scaffold or heart valve support system would be fixed either on the ventricular or arterial side of the valve with fixation thereto. In the case of the aortic valve, if placed in the aorta, the scaffold or valve support system is perhaps best placed in a sub-coronary ostial position so as not to obstruct coronary flow. In this application of the invention, the hooks, barbs or other appropriate components for grasping the valves are modified to grasp or entrap the leaflets from the convex side of the leaflet, thereby ensnagging or otherwise achieving leaflet fixation on or through the ventricular surface or coaptation surface/margin of the valve.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic longitudinal cross-sectional view of a delivery catheter containing an implantable device in accordance with the present invention, in a collapsed, low profile configuration to facilitate minimally invasive access.

Figure 2 is a schematic side elevational view of a tubular tether surrounding a proximal portion of an elongate tension member or tensile coupling element provided at a free or distal end with an entrainment element in the form of a grappling hook.

Figure 3 is a schematic side elevational view of the delivery catheter of Figure 1 as advanced through a vascular system of a subject to a native heart valve.

Figure 4 is a schematic side elevational view similar to Figure 3, showing a multiplicity of hook-like entrainment or capture elements on tensile coupling members as shown in Figure 2, advanced inside the native valve of Figure 3 into a heart chamber or blood vessel.

Figure 5 is a schematic side elevational view similar to Figures 3 and 4, showing the delivery catheter retracted back across the native heart valve with the hooks and tension members remaining in place.

Figure 6 is a schematic perspective or side elevational view similar to Figures 3-5, showing partial extrusion or ejection of a neo-annulus scaffold or valve support member from the delivery catheter, while hooks and tension elements remain in place adjacent to the native valve leaflets.

Figure 7 is a schematic perspective view similar to Figures 3-6, showing the scaffold expanded in a heart chamber or blood vessel, ready for manipulation or positioning by a series of tethers like the tether of Figure 2.

Figure 8 is a schematic perspective view similar to Figures 3-7 showing initial purchase or entrainment of the native heart valve leaflets by the hooks of the tensile coupling elements, which condition of initial entrainment still allows normal or near normal valve function.

Figure 9 is a schematic perspective view similar to Figures 3-8, showing a prosthetic or bio-prosthetic replacement valve deployed into an orifice of the scaffold or valve support member.

Figure 10 is a schematic perspective view similar to Figures 3-9, showing a neo-annulus/replacement valve complex advanced towards the orifice of the native valve by exertion of a retractive or proximally directed force on the tensile coupling elements and a simultaneous exertion of a pushing or distally directed force on the tubular tethers.

Figure 11 is a schematic perspective view similar to Figure 10, showing further advancement of the neo-annulus/replacement valve complex towards the orifice of the native valve.

Figure 12 is a schematic perspective view similar to Figures 3-11, showing a seating of the neo-annulus/replacement valve complex into the orifice of the native valve and full retraction of the tension or coupling members.

Figure 13 is a schematic perspective view similar to Figure 12, showing the neo-annulus/replacement valve complex seated the orifice of the native valve after removal of the tethers and severing of the tensile coupling elements.

Figure 14 is a schematic perspective or side elevational view, showing a step of an alternative valve implantation procedure, wherein a ring-shaped neo-annulus scaffold or valve support member is provided with a plurality of elongate flexible suspension elements that are fixed to the heart or blood vessel wall via respective removably attached deployment tethers that deliver staples or clips.

Figure 15 is a schematic perspective view similar to Figure 14, showing the neo-annulus scaffold supported by the deployed elongate suspension elements of Figure 14, and with the deployment tethers of Figure 14 removed, ready for valve capture and replacement valve deployment, followed by advancement of the complex into the native valve orifice.

Figure 16 is a partial schematic perspective view similar to Figure 14, showing a detail of an alternative, auto-fixation, method of attachment of a suspension line to a heart or vessel wall.

Figure 17 is a schematic plan view of a native mitral valve, showing valve commissures.

Figure 18 is a schematic plan view similar to Figure 17, showing a ring-shaped neo-annulus scaffold in place over the native mitral valve. Hooks for valve leaflet capture and the associated tensile coupling elements are visible through the orifice of the neo-annulus scaffold while the positioning tethers of Figure 2 extend between the delivery catheter and

the neo-annulus, the lumen of the catheter being shown in cross-section.

Figure 19 is a schematic plan view similar to Figures 17 and 18, depicting the neo-annulus scaffold in position abutting the valve leaflets and with a prosthetic or bio-prosthetic replacement valve deployed, further depicting commissures leaving gaps in the seal around the neo-annulus, resulting in a perivalvular leak.

Figure 20 is a partial schematic perspective view of the neo-annulus scaffold and replacement valve of Figure 19 in position abutting the native-valve leaflets, illustrating a gap at a commissure, and also schematically illustrating locks on the tensile coupling elements holding them in place relative to the neo-annulus.

Figure 21 is a series of three side elevational views of a tissue approximation clip or anchor in three configurations relative to apposed valve leaflets, initially inserted through a commissure gap, then retracted causing apposition of the leaflets and a filling of the gap, and finally with prongs bent for permanent placement.

Figure 22 is a partial schematic perspective view similar to Figure 20, showing the anchor-shaped clip of Figure 21 deployed for leaflet-edge approximation.

Figures 23A and 23B are a pair of partial schematic cross-sectional views of an annulus or ring-shaped valve support member, a tether and a tensile coupling element, Figure 23A showing a collapsed bladder-like component, along with an inflation-port, Figure 23B showing the bladder-like component after inflation.

Figure 24 is a schematic partial side elevational view of a neo-annulus scaffold in apposition with a captured valve leaflet with the inflatable component of Figures 23A and 23B in an expanded configuration sealing a line of contact and with infusion tube and port still attached.

Figure 25 is a partial schematic perspective view similar to Figure 22, showing a bladder-like sealing component disposed around a periphery of the neo-annulus scaffold in a deflated insertion configuration.

Figure 26 is a partial schematic perspective view similar to Figure 25, showing the bladder-like sealing component in an expanded sealing configuration, covering or closing a gap between valve leaflets.

Figure 27 is a schematic side elevational view of ratchet-type locking components provided on the neo-annulus scaffold and the distal end of a tensile coupling element to allow only one-way excursion of the tensile coupling element and its appended valve-capture or entrainment element (not shown), the tether being pushed in the distal direction and the tensile coupling element being pulled in the proximal direction to clamp the neo-annulus scaffold and attached replacement valve to the valve leaflets.

Figures 28A and 28B are a schematic perspective view and a schematic longitudinal cross-sectional view, respectively, showing another embodiment of a ratchet mechanism.

Figure 29 is a schematic perspective view of a neo-annulus scaffold with collapsed

perimetral closure bladder, tensile coupling elements with distal hooks entrained to the ends or edges of native valve leaflets, and tubular tethers extending from the distal end of a delivery catheter and holding the scaffold in position for installation.

Figure 30 is a schematic perspective view similar to Figure 29, showing a replacement valve mounted to the neo-annulus scaffold.

Figure 31 is a schematic plan view of the neo-annulus scaffold of Figures 29 and 30 in place above the native mitral valve with native valve capture and the "sewing ring" or closure bladder inflated, but with the replacement valve omitted.

Figure 32 is a schematic side elevational view of a helical fastener with a truncated sleeve, which is slidably disposed over a scaffold-positioning tether, in accordance with the present invention.

Figure 33 is a schematic perspective or isometric view of a helical fastener similar to that of Figure 32 sliding over a tether. Figure 33 also depicts a portion of a pusher sleeve or tube.

Figure 34 is a schematic partial cross-sectional view of the helical fastener of Figure 32 juxtaposed to a heart wall and a margin of a valve-support scaffold.

Figure 35 is a schematic partial cross-sectional view similar to Figure 34, showing the helical fastener advanced into the heart wall, with the fastener straddling the margin of the scaffold.

Figure 36 is a schematic partial cross-sectional view similar to Figure 35, showing the fastener partially embedded in the heart wall with the pusher sleeve or tube withdrawn, but the tether still attached to the scaffold margin.

Figure 37 is a schematic partial cross-sectional view similar to Figure 35, showing the fastener partially embedded in the heart wall and holding the scaffold in place, but with the tether removed, this view representing the ultimate state of scaffold fixation.

Figure 38 a schematic perspective or isometric view of a valve-support scaffold in an expanded configuration and a plurality of positioning tethers.

Figure 39 is a view similar to Figure 38, showing a pusher sleeve or tube advanced over a tether and in contact with a helical fastener at the margin of the valve-support scaffold, for deployment of the fastener into a heart or blood vessel wall.

Figure 40 is a schematic side elevational view of an alternative, two-pronged staple for fastening a margin of a valve-support scaffold to a heart or blood vessel wall.

Figure 41 is a schematic cross-sectional view of the staple of Figure 40 with the prongs partially inserted into a heart or blood vessel wall over a margin or rim element of a valve-support scaffold or frame.

Figure 42 is a schematic cross-sectional view similar to Figure 41, showing the prons or legs of the staple in an angled-apart or expanded configuration to create fixation.

Figure 43 is a schematic cross-sectional view of a second alternative staple

configuration wherein the tips turn in to create fixation.

Figure 44 is a schematic cross-sectional view similar to Figure 43, shows a prong of the staple provided with a removal-prevention barb.

Figure 45 is a schematic perspective or isometric view of a valve retrieval system, for capturing leaflets of a natural atrial valve and indirectly capturing the cords (not shown), showing the natural valve in a closed state.

Figure 46 is a schematic perspective or isometric view similar to Figure 45, showing the valve in an opened state.

Figure 47 is a schematic perspective or isometric view similar to Figures 45 and 46, showing the valve retrieval system advanced through the open valve.

Figure 48 is a schematic perspective or isometric view similar to Figure 47, showing the valve closed around the valve retrieval system.

Figure 49 is a schematic perspective or isometric view similar to Figure 48, showing the retrieval system engaging the valve, with the delivery system retracted.

Figure 50 is a schematic perspective or isometric view similar to Figure 49, showing a pair of leaflet-capture tethers or the retrieval system shifted apart to engage and curl or otherwise engage and/or retract the leaflets

Figure 51 is a schematic perspective or isometric view similar to Figure 50, showing the retrieval system delivery apparatus removed.

Figure 52 is a view similar to Figure 51, showing the tethers of the retrieval system drawn through a valve-receiving neo-annulus or aperture of a valve-support scaffold as a prosthetic valve is deployed into the neo-annulus of the scaffold.

Figure 53 is a view similar to Figure 52, showing the tethers of the valve retrieval system completely engaged with the valve leaflets and fixing the leaflets to the valve-support scaffold as well as to the implanted prosthetic valve.

Figure 54 is a view similar to Figure 52, showing the native valve leaflets fully retracted and attached to the scaffold and the prosthetic heart valve and with locking apparatuses connected on the tethers of the heart valve retrieval system to reinforce fixation of those tethers to the scaffold and the deployed prosthetic valve.

Figure 55 is a schematic perspective or isometric view of the helical fixation device or fastener of Figure 32, showing a pin disposed in a cap of the helical fixation device, which, when advanced into the heart or blood vessel wall, prohibits untwisting of the helical fastener.

Figure 56 is a view similar to Figure 55, showing the pin in a deployed or advanced position.

Figure 57 is a schematic perspective view of an expanded valve-support scaffold extended via positioning tethers out of a delivery catheter, showing the catheter in a pair of configurations illustrating steerability of the catheter tip.

Figure 58 is a schematic perspective or isometric view of a portion of a leaflet entrainment device in accordance with the present invention.

Figure 59 is a schematic perspective or isometric view of a portion of a modified leaflet entrainment device in accordance with the present invention.

Figure 60 is a schematic perspective or isometric view of a valve retrieval system inserted in a retrograde direction through an opened aortic valve.

Figure 61 is a schematic perspective or isometric view similar to Figure 60, showing the aortic valve closed around the valve retrieval system.

Figure 62 is a schematic perspective or isometric view similar to Figures 60 and 61, showing the retrieval system engaging the valve.

Figure 63 is a schematic perspective or isometric view similar to Figures 60-62, showing a pair of leaflet-capture tethers or the retrieval system shifted apart and engaging and curling the leaflets.

Figure 64 is a schematic perspective or isometric view similar to Figures 60-63, showing the retrieval system delivery apparatus removed the tethers of the retrieval system drawn through a valve-receiving neo-annulus or aperture of a valve-support scaffold, and a prosthetic valve deployed into the neo-annulus of the scaffold.

DEFINITIONS

The word "tether" is used herein to denote an elongate member that extends from outside a patient to an implantable device inside the patient, especially but not necessarily within the vascular system. A tether is used to remotely manipulate and position the implantable device within the patient and may also be used to implement attachment of the implantable device to organic tissues of the patient. It is contemplated that a tether is normally detachable from the implantable device once implantation has been secured. A tether may be a wire made of a metallic or metal alloy material and is capable of transmitting compressive, tensile and torsional forces as required.

The terms "scaffold" and "neo-annulus" are used interchangeably herein to denote an implantable device or structure that serves as a framework for receiving a prosthetic valve and anchoring the valve to the patient at the site of a malfunctioning native valve. A scaffold or neo-annulus is preferably delivered to the operative site via a catheter. Consequently, the scaffold or neo-annulus must be flexible or collapsible for insertion into the patient. Once the scaffold or neo-annulus is ejected from the catheter into the patient, the scaffold or neo-annulus expans to a predetermined use configuration suitable for receiving, seating and attaching to a prosthetic or bio-prosthetic valve. A scaffold or neo-annulus as decribed herein defines an orifice, preferably circular, for receiving a prosthetic or bio-prosthetic valve.

The term "prosthetic" as applied to a valve herein includes bio-prosthetic valves.

The term "force-transmitting and fluid-sealing contact" as used herein with reference to the implantation of a scaffold or neo-annulus in juxtaposition with or apposition to native

valve leaflets means in part that the scaffold or neo-annulus is attached at least indirectly to the native valve leaflets so as to enable the transmission of operative natural valve forces at least in part over the native valve to the scaffold or neo-annulus and the prosthetic valve attached thereto. The term "force-transmitting and fluid-sealing contact" also means that the implanted scaffold or neo-annulus is effectively sealed relative to the natural valve so that blood flow occurs essentially solely through the prosthetic valve upon completion of the implantation procedure. Sealing may occur wholly or in part because of direct contact between the scaffold or neo-annulus and the native valve leaflets or between the scaffold or neo-annulus and the cadio-vascular wall about the native valve. A seal may be effectuated wholly or in part because of the use of an ancillary sealing element or elements such as staples, clips or sutures or one or more inflatable bladders that close off potential fluid flow channels about the scaffold or neo-annulus.

The term "cadio-vascular wall" is used herein to denote the inner surface of a heart chamber or a blood vessel into which a prosthetic valve and its associated scaffold or neo-annulus is implanted.

The terms "tensile coupling element" and "tension member" and variations thereof are used herein to denote an elongate member such as a wire which may be pushed or pulled and thus supports both compressive and tensile forces, as well as torsional forces and which in part remains in a patient connecting a scaffold or neo-annulus to a patient under tension.

The terms "distal" and "distally directed" are used herein to denote a direction extending from an operator such as a surgeon, who is outside a patient, towards the patient and more particularly towards a valvular structure inside a patient. Concomitantly, the terms "proximal" and "proximally directed" denote a direction extending towards an operator such as a surgeon from a patient and more particularly from a valvular structure inside a patient.

DETAILED DESCRIPTION

The present invention provides devices and associated methodology for attaching a valve-supporting scaffold or frame member to a subject, particularly to natural valve leaflets of a native heart or vessel valve of the subject. Such a valve-supporting scaffold and methods related thereto are disclosed in U.S. Patent Application Publication No. 2010/0262232, the disclosure of which is hereby incorporated by reference.

As illustrated in Figure 1, a delivery system for an implantable valve support device 610 comprises a delivery catheter 612, which contains the implantable device in a collapsed low profile configuration to facilitate minimally invasive access. Figure 1 shows a plurality of valve-leaflet entrainment or capture elements 614 in the form of hooks, e.g., grappling hooks, or barbs. As illustrated in Figure 2, each leaflet entrainment element 614 is carried at the free or distal end of an elongate flexible tensile coupling element 616. Each tensile coupling element 616 extends through a respective tubular positioning tether 618 that is

removably attached at its distal end to a locking element 620 in turn connected to a neo-annulus or scaffold 622 that receives and supports a prosthetic or bio-prosthetic valve. Positioning tether 618 surrounds a proximal portion 624 of tensile or tensile coupling member 616. As discussed in detail hereinafter, in a prosthetic-valve implantation procedure, neo-annulus or scaffold 622 is moved towards a native valve by exerting a distally directed force 626 on tubular positioning tether 618 while exerting a proximally directed force 628 on tensile coupling element 616.

Figure 3 shows delivery catheter 612 as advanced through a vascular system of a subject to a native heart valve HV having a pair of valve leaflets VL1 and VL2. A distal tip 630 of catheter 612 is located in or proximate to an orifice VO between valve leaflets VL1 and VL2. At that juncture of a valve implantation procedure, hook-like entrainment or capture elements 614 and distal end portions of tensile coupling elements 16 are ejected from the distal tip 630 of delivery catheter 612, as depicted in Figure 4. Then, as shown in Figure 5, delivery catheter 612 is retracted back across the native heart valve HV with the hooks 614 and tension members 616 remaining in place.

Figure 6 shows a subsequent step of a valve implantation procedure, in particular a partial extrusion or ejection of neo-annulus or scaffold 622 from delivery catheter 612. Hooks 614 and tensile coupling elements 616 remain in place adjacent to the native valve leaflets VL1 and VL2. Figure 7 shows neo-annulus or scaffold 622 fully ejected from catheter 612 and expanded in the heart chamber or blood vessel. Multiple positioning tethers 618 extend to respective locks 620 (Figure 2) and support the expanded neo-annulus or scaffold 622 during the implantation procedure. Tensile coupling elements 616 extend from respective positioning tethers 618 at the periphery of neo-annulus or scaffold 622. Leaflet-entrainment hooks 614 dangle loosely within or beyond the native valve orifice VO.

As shown in Figure 7, the expanded neo-annulus or scaffold 622 takes the form of a ring which defines a valve-receiving circular orifice 623. Neo-annulus scaffold 622 is preferably flexible for at least a given time after ejection from delivery catheter 612 so as to allow manipulation and reconfiguration after delivery, but also relatively inelastic so that a radially expanded valve 634 (Figures 9 et seq.) does not distort it. Scaffold 622 may be constructed of a braided or monofilament metal or other appropriate synthetic or naturally occurring material with the appropriate physical characteristics. Alternatively, scaffold 622 made be made of nitinol optionally with a temperature-induced memory by which the scaffold assumes a substantially fixed ring shape after ejection from the delivery or deployment catheter 612.

After the ejection of neo-annulus or scaffold 622, tensile coupling elements 616 are manipulated from outside the patient to bring hooks 614 into engagement with the edges (not separately designated) of valve leaflets VL1 and VL2, as depicted in Figure 8. This initial entrainment allows normal or near normal valve function. Subsequently, as shown in

Figure 9, prosthetic or bio-prosthetic valve 634 is seated in neo-annulus orifice 623 (see Figure 7) and attached to scaffold 622 to form a neo-annulus/replacement valve complex 636.

Figure 10 depicts scaffold 622 with the mounted valve 634 moved closer to native valve HV. This change in position of neo-annulus/replacement valve complex 636 is effectuated by pushing positioning tethers 618 in a distal direction, as indicated by force arrow 626 in Figure 2, while simultaneously pulling tensile coupling elements 616 in a proximal direction, as indicated by force arrow 628 in Figure 2.

Figure 11 is a schematic perspective view similar to Figure 10, showing further advancement of neo-annulus/replacement valve complex 636 towards the orifice VO of the native valve HV. After a final advancement of neo-annulus/replacement valve complex 636, depicted in Figure 12, the neo-annulus/replacement valve complex is seated into the orifice VO of the native valve HV and tensile coupling elements are fully retracted to curl the lips or edges of valve leaflets VL1 and VL2.

Subsequently, as depicted in Figure 13, positioning tethers 618 are removed or detached from the implanted neo-annulus/replacement valve complex 636 and tensile coupling elements 616 are severed at locks 620 (Figure 2). In the completed implantation, neo-annulus/replacement valve complex 636 is held by tensile coupling elements 616 and entrainment hooks 614 in a fluid sealing engagement with valve leaflets VL1 and VL2. This mode of implantation ensures that the valve securing forces exerted by the chordae tendineae.

Figures 14-16 depict steps in a modified implantation procedure wherein neo-annulus or scaffold 622 is provided at spaced intervals around its circumference with a plurality of flexible elongate tensile suspension elements 638 that are attachable at their free ends 640 to a wall CVW of the heart or a blood vessel (collectively, "cardio-vascular wall"). Suspension members 638 are manipulated via respective deployment tethers 642 that extend from delivery catheter 612 or a separate deployment catheter (not illustrated) and detachably attach to the suspension members at free ends 640 thereof. Typically, free ends 640 of suspension members 638 are coupled to wall CVW after the ejection of scaffold 622 from catheter 612 but before the moving of neo-annulus/replacement valve complex 636 into engagement with valve leaflets VL1 and VL2, and preferably before the seating of prosthetic valve 634 in orifice 623 of neo-annulus or scaffold 622.

Scaffold 622 is optionally provided with suspension elements 638, which are extendible radially to attach to the heart or blood vessel wall CVW near the native valve HV for which replacement is intended. Suspension elements 638 appear like spider legs, or as ring-topped, flattened tripod (in an instance wherein three such elements are used). Suspension elements 638 may be constructed of a spring-like material and are curved to allow for fixation to heart or blood vessel wall CVW of variable contour and also allow for

excursion of the neo-annulus scaffold 622 toward the valve HV as necessary.

Figure 15 shows neo-annulus scaffold 622 supported by the deployed elongate suspension elements 638 of Figure 14, and with deployment tethers 642 removed. Scaffold 622 is ready for capture of valve leaflets VL1 and VL2 by entrainment hooks 614 and for deployment of prosthetic valve 634 (not shown), followed by advancement of the complex 636 into the native valve orifice VO.

Figure 16 depicts a detail of an alternative, auto-fixation, method of attachment of a suspension line 638 to cardio-vascular wall CVW. Suspension line 638 is provided at a free end with a barb 644 that anchors the suspension line to the cardiovascular wall CVW. Deployment tether 642 is removably coupled to suspension line 638 to permit the forceful insertion of barb 644 into the tissues of wall CVW and the subsequent detachment of tether 642 from suspension line 638.

Figure 17 is a schematic plan view of native mitral valve HV, showing valve commissure gaps VC1 and VC2 between valve leaflets VL1 and VL2. Figure 18 illustrates ring-shaped neo-annulus scaffold 622 in place over the native mitral valve HV. Hooks 614 for capture of valve leaflets VL1 and VL2 and the associated tensile coupling elements 616 are visible through the orifice 623 of neo-annulus scaffold 622 while the positioning tethers 618 of Figure 2 extend from delivery catheter 612 to the neo-annulus scaffold, the lumen 646 of the catheter being visible in cross-section. As shown in Figures 19 and 20, with neo-annulus scaffold 622 in position abutting the valve leaflets VL1 and VL2 and prosthetic or bio-prosthetic replacement valve 634 deployed, commissure gaps VC1 and VC2 are open at the periphery of the neo-annulus, resulting in a perivalvular leak. Two approaches for closing gaps VC1 and VC2 are discussed below.

Figure 20 also schematically illustrates locks 620 cooperating with the tensile coupling elements 616 to hold them in place relative to neo-annulus or scaffold 622.

Figure 21 is a series of three side elevational views of a tissue approximation clip or anchor 650 in three configurations relative to apposed valve leaflets VL1 and VL2. Clip or anchor 650 is initially inserted in a distal direction 652 through a commissure gap VC1 or VC2 (only VC2 shown). Then clip or anchor 650 us retracted in a proximal direction 654, causing apposition of the leaflets and a closing of the gap. Finally prongs 656 of clip or anchor 650 are bent downwardly at 658 for permanent placement.

Figure 22 is a partial schematic perspective view similar to Figure 20, showing anchor-shaped clip 650 deployed for leaflet-edge approximation. Typically, one or more clips or anchors 650 are deployed after the locking of neo-annulus/replacement valve complex 636 to the valve leaflets VL1 and VL2. However, one or more clips or anchors 650 may alternatively deployed prior to the engagement or locking of the neo-annulus/replacement valve complex 636 to the valve leaflets.

In an alternative method for closing commisure gaps VC1 and VC2 (see Figure 31),

neo-annulus or scaffold 622 is provided along an other periphery with a collapsed bladder-like component 660, as depicted in Figure 23A. An inflation tube or port member 662 extends to collapsed bladder 660 for feeding thereto a fluid such as carbon dioxide, saline solution, a liquid polymer, a polymerizable monomer composition, etc., thereby expanding the collapsed bladder or balloon 660 to an enlarged configuration 664 shown in Figure 23B. The expanded bladder configuration 664 is also depicted in Figures 24 and 26, while Figure 25 shows the collapsed insertion configuration of balloon or bladder 660. As depicted in Figure 26, expanded bladder configuration 664 covers and closes commisure gaps VC1 and VC2. Typically, as illustrated in Figures 25 and 26, the bladder 660, 664 is an annular member extending circumferentially about the outer periphery of neo-annulus or scaffold 622.

Figure 27 is a schematic side elevational view of ratchet-type locking components 620 and 666 provided on the neo-annulus scaffold 622 and distal ends of tensile coupling elements 616 to allow only one-way excursion of the tensile coupling elements and the appended valve-capture or entrainment elements 614 (see other figures). Locking component 666 is a series of tapered teeth 668 each having, for example, a frusto-conical form (Figure 2). In that case, locking component 620 is a block provided internally with one or more tapered passageway sections 670 that are geometrically congruent with teeth 668. Tensile element 616 may be pulled in the proximal direction 628 while positioning tether 618 is pushed in the distal direction 626, which moves locking component 620, and accordingly scaffold 622 and neo-annulus/replacement valve complex 636, in the distal direction relative to tensile coupling element 616. However, the shapes of teeth 666 and passageway sections 670 prevent an opposite relative motion of tensile coupling element 616 and neo-annulus/replacement valve complex 636. Ratchet-type locking components 620 and 666 thus enable a clamping of the neo-annulus scaffold 622 and attached replacement valve 634 to the valve leaflets VL1 and VL2.

Figures 28A and 28B show another embodiment of a ratchet mechanism wherein lock 620 is provided internally with a pivotably mounted latch or détente 672 having a sharp end 674 pointed in a proximal direction, towards tether 618. Latch or détente 672 permits motion of tensile coupling element 616 in the proximal direction 28, that is, towards tether 618 but prevents the opposite motion.

Figure 29 depicts neo-annulus scaffold 622 with collapsed perimetral closure bladder 660, tensile coupling elements 616 with distal hooks 614 entrained to the ends or edges of native valve leaflets VL1 and VL2, and tubular tethers 618 extending from the distal end of a delivery catheter 612 and holding the scaffold in position for installation.

Figure 30 is a schematic perspective view similar to Figure 29, showing replacement valve 634 mounted to the neo-annulus scaffold 622.

Figure 31 shows neo-annulus scaffold 622 in place above the native mitral valve HV

with native valve leaflets VL1 and VL2 captured and the "sewing ring" or closure bladder 660 in its inflated configuration 664 but with the replacement valve 634 omitted for clarity.

Suspension elements 638, as well as the neo-annulus or scaffold 622, may be covered or coated with a substance to enhance tissue ingrowth, prevent clot or blood adhesion, may be drug eluting, heparin or other substance bonding, or or otherwise be constructed of a material that enhances tissue ingrowth, prevent clot or blood adhesion.

The implantation device and associated method described above are designed in such a way as to enhance delivery by construction of the scaffold so that valve-capture elements 614, suspension elements 638, if used, peri-valvular inflatable or gap-closure devices 650 and 660, if used, are incorporated into the neo-annulus 622 such that serial emergence from the delivery system 612 simplifies placement of the entire system. Combining valve deployment with capture of the native valve leaflets VL1 and VL2 may create a minimal risk of valvular stenosis or insufficiency. Further, the design of the device transfers all cardiac forces onto the native valve HV. In the case of AV valves, the scaffold or valve support device 622 is at least indirectly secured to chordae tendineae, and therefore, the papillary muscles of the heart. Therefore such a device can distribute forces to the prosthetic valve 634 similar to those typical of the normal, native valve.

Figures 32 et seq. below describe alternative methods and devices for implanting a prosthetic or bio-prosthetic valve in a heart chamber or blood vessel. Fastener or fixation devices 400, 428, and 436 described hereinafter are useful for attaching suspension elements 438 to cardio-vascular wall CVW.

As illustrated in Figure 32, a fastener or fixation device 400 for coupling a valve-supporting scaffold 402 (Figures 38 and 39) comprises a pair of helical prongs or legs 404 each attached at one end to a cap or head 406 in the form of a disk. As illustrated in Figure 34, disk 406 is provided with a hole 408, which is traversed by a scaffold-positioning tether 410 (Figures 33, 34, 35) so that the fastener or fixation device 400 is slidable along the tether. During a deployment operation, a pusher member 412 in the form of an elongate sleeve or tube (only a distal end portion thereof shown in the figures) engages cap or head 406 to press fastener 400 to a distal end of tether 410 and into organic tissues, specifically a heart chamber or vessel wall 414. Once distal tips 416 of prongs or legs 404 enter the heart chamber or vessel wall 414, further distal motion of pusher member 412 induces fastener to turn about its longitudinal axis 418 (Figure 32), twisting the fastener deeper into the organic tissues. Prongs or legs 404 straddle an outer margin or outer rim element 420 (Figures 34-37) of scaffold 402, with one of the prongs or legs passing through a membrane 422 that extends between margin 420 and an inner rim element or neo-annulus 424 of the scaffold. Prong tips 416 enter the heart or vessel wall on the opposing sides of margin 420, and the prongs or legs 404 cooperate with the organic tissue in a camming motion to induce rotation of the fastener 400.

Insertion of fastener 400 is complete when cap or head 406 comes into contact with margin 420, as shown in Figure 35. Pusher member 412 is then withdrawn (compare Figure 36 with Figure 35). Tether 410 is also detached from scaffold 402 and withdrawn (Figure 37). Pusher member 412 may be extracted from the heart or vessel and from the patient prior to the detachment and extraction of tether 410. Alternatively, tether 410 may be detached first (e.g., by a twisting of the tether), with a subsequent simultaneous extraction of the tether and pusher member 412.

Figure 38 shows scaffold 402 after it has been ejected from a delivery catheter 426 and opened from a collapsed insertion configuration (not shown) to the illustrated expanded deployment configuration. A plurality of tethers 410, detachably linked at their distal ends to margin 420 of scaffold 402 at spaced locations theralong, includes three primary tethers 410a and optionally several secondary tethers 410b. Primary tethers 410a are manipulated to position margin 420 and concomitantly scaffold 402 into a desired position and orientation inside a target heart chamber or vessel. Fasteners 400 are initially deployed along the primary tethers 410a (see Figure 39) to connect margin 420 to heart chamber or vessel wall 414 at three respective locations. Further fasteners 400 may be subsequently deployed along the secondary tethers 410b.

As depicted in Figures 40-42, an alternative fastener or margin fixation device 428 is a staple having two prongs or legs 430 each attached at one end to a cap or head 432 in the form of a perforated disk slidably traversed by tether 410. Prongs or legs 430 each exhibit a shallow S-shape with an outwardly turned tip 434, the two prongs being mirror images of one another. Tips 434 cause prongs or legs 430 to splay outwardly during an insertion operation, as shown in Figure 42. This divergence or opening of the staple prongs 430 serves to anchor fasteners 428 in a heart chamber or vessel wall 414.

As illustrated in Figures 43 and 44, another alternative fastener or margin fixation device 436 is a staple having two prongs or legs 438 each attached at one end to a cap or head 440 again in the form of a perforated disk slidably traversed by tether 410. Prongs or legs 438 each have a slightly arcuate proximal portion 442 attached to cap or head 440 and an inwardly dog-legged distal end 444. Distal ends 444 cause prongs or legs 438 to crimp inwardly during an insertion operation. As shown in Figure 44, one or both prongs 438 may carry a rearwardly oriented barb or hook 446 for providing enhanced resistance to removal of the fastener 436 from the heart or vessel wall 414.

Figure 45 depicts a valve retrieval system 448 comprising an introducer catheter 450 and a plurality of tethers 452 deployed via the catheter and provided at their free ends with capture hooks or barbs 454 for entraining leaflets 456 of a natural atrial valve 458 and indirectly capturing the cords (not shown). Valve retrieval system 448 further includes a tether guide member 460, which maintains tethers 452 in a suitably arranged or distributed array. To that end, tether guide member may be provided with angularly spaced grooves or

passageways for guiding the respective tethers 452. Valve retrieval system 448 is inserted into the patient after the installation of valve-supporting scaffold 402 and prior to the seating of a prosthetic valve 462 (Figures 52-54) in neo-annulus 424.

Upon an opening of the natural valve 458 as depicted in Figure 46, valve retrieval system 448 is moved in a distal direction and inserted trough the open valve, as depicted in Figure 47. The natural valve then closes over valve retrieval system 448 as shown in Figure 48. At that juncture, valve retrieval system 448 is slightly retracted so that the hooks or barbs 454 are juxtaposed to the valve leaflets 456 as indicated in Figure 49. Tethers 452 and tether guide member 460 are then manipulated to insert hooks or barbs 454 into valve leaflets 456. As indicated in Figure 50, the distal ends of tethers 452 including hooks or barbs 454 shift laterally or outwardly to capture and entrain leaflets 456. This movement of tethers 452 is implemented via tether guide member 460. To that end, the grooves or channels in tether guide member 460 that guide tethers 452 may be formed with camming surfaces such as humps that move the tethers laterally outwardly upon a longitudinal shifting of the guide member 460 relative to the tethers.

After the ensnaring or snagging of leaflets 456 by hooks or barbs 454, catheter 450 and tether guide member 460 are withdrawn, as shown in Figure 51. Then, as depicted in Figure 52, prosthetic valve 462 is inserted inside a ring of tethers 452 so that the leaflet-entraining tethers are clamped between neo-annulus 424 of scaffold 402 and the prosthetic valve. Tethers 452 are further retracted at that juncture to curl leaflets 456 and constrain them about the margin 420 of scaffold 402, as illustrated in Figure 53. Then tethers 452 are severed (Figure 53) and locks 464 are attached to the severed tether ends (Figure 54).

As illustrated in Figures 55 and 56, fastener 400 may be provided with a pin 466 movably coupled to cap 406 for enabling a locking of the fastener to heart chaber or vessel wall 414. Upon completed insertion of prongs 404 into heart chamber or vessel wall 414, pin 466 is moved from a retracted neutral position (Figure 55) to an advanced locking losition (Figure 56). In its advanced position, pin 466 prevents fastener 400 from rotating or untwisting from its inserted position clamping margin 420 to the heart or vessel wall.

Figure 57 shows how delivery catheter 426 has a steerable distal end 468 which may assume any of a plurality of orientations 468a, 468b, etc. relative to a main body 470 of the catheter, thereby facilitating a placement of scaffold 402.

Figure 58 depicts a distal end portion of a leaflet entrainment device 472 having four hooks or barbs 474 that are actively or passively released when engaged with a valve leaflet or cord.

Figure 59 depicts a leaflet entrainment device 476 with two subassemblies 478 and 480 including respective tubular delivery members 482 and 484 and pairs of hooks or barbs, 486 and 488. Tubular delivery members 482 and 484 are spring biased to separate as illustrated after emergence from a delivery catheter 490.

Figures 60-64 depict a series of steps similar to those described hereinabove with reference to Figures 45-54, applied in a retrograde procedure to capture leaflets 500 of an aortic valve 502 and attach the captured leaflets to an implanted scaffold 504 and a prosthetic valve 506 (Figure 64) which is seated in a neo-annulus 508 of the scaffold. The procedure of Figures 60-64 is particularly pertinent in solving a problem called "aortic insufficiency" where there is no calcium, so, like as in the case of the mitral valve, an expanding, radial-force valve cannot be used. This disease is a common occurrence as a result of LVAD (left ventricular assist device) placement.

As shown in Figure 60, a valve retrieval system 510 which is similar if not identical to system 448, comprises the same components, namely, introducer catheter 450 and tethers 452 with capture hooks or barbs 454 at the free ends thereof. Hooks or barbs 454 are effective in the procedure of Figures 60-64 to entrain leaflets 500 of aortic valve 502. Again, tether guide member 460 maintains tethers 452 in a suitably arranged or distributed array. Valve retrieval system 448 is inserted into the aorta after the installation of valve-supporting scaffold 502 and prior to the seating of prosthetic valve 506 in neo-annulus 508.

Upon an opening of the aortic valve 502 as depicted in Figure 60, valve retrieval system 448 is moved retrograde in the aorta (not separately labeled) and inserted through the open valve, as depicted. The aortic valve 502 then closes over valve retrieval system 448 as shown in Figure 61. At that juncture, valve retrieval system 448 is slightly retracted so that the hooks or barbs 454 are juxtaposed to the valve leaflets 500 as indicated in Figure 62. Tethers 452 and tether guide member 460 are then manipulated to insert hooks or barbs 454 into valve leaflets 500. As indicated in Figure 63, the distal ends of tethers 452 including hooks or barbs 454 shift laterally or outwardly to capture and entrain leaflets 500. This movement of tethers 452 is implemented via tether guide member 460, as described above with references tro Figures 45-54.

After the ensnaring or snagging of aortic leaflets 500 by hooks or barbs 454, catheter 450 and tether guide member 460 are withdrawn, prosthetic valve 506 is inserted inside a ring of tethers 452 so that the leaflet-entraining tethers are clamped between neo-annulus 508 of scaffold 502 and the prosthetic valve. Tethers 452 are further retracted at that juncture to curl leaflets 456 and constrain them about the margin 512 of scaffold 502, as illustrated in Figure 64. Then tethers 452 are severed. Locks 464 may be attached to the severed tether ends, as discussed hereinabove with reference to Figure 54.

In another approach constituting a variation of the procedure described in U.S. Patent Application Publication No. 2010/0262232 and International Patent Application No. PCT/US2010/001077, a scaffold or valve support device with a central orifice defining annulus and a preferably flexible margin or perimeter element is attached to the atrial wall. One then waits a few (3-6) weeks for tissue growth to bind the scaffold or valve support device to the atrial wall. At that juncture a prosthetic or bioprosthetic valve is seated in the

orifice.

Accordingly, fastening elements are provided herein or in U.S. Patent Application Publication No. 2010/0262232 and International Patent Application No. PCT/US2010/001077 for attaching said scaffold or valve support device either (1) to heart or blood vessel tissue adjacent to a native heart valve, (2) at least indirectly to leaflets of a native valve of a patient, or (3) to both adjacent tissue and directly or indirectly to heart valve tissue. Preferably, the attachment is such that the scaffold or valve support device potentially is in effective force-transmitting and effective perivalvular fluid-sealing contact with the target native valve and substantially fixedly attached to the patient.

Although the invention has been described in terms of particular embodiments and applications, one of ordinary skill in the art, in light of this teaching, can generate additional embodiments and modifications without departing from the spirit of or exceeding the scope of the claimed invention. For instance, instead of being attached directly to the valve leaflets VL1 and VL2, neo-annulus/replacement valve complex 36 of suitable dimensions may be attached in whole or in part to the cardio-vascular wall CVW about native valve HV. Accordingly, it is to be understood that the drawings and descriptions herein are proffered by way of example to facilitate comprehension of the invention and should not be construed to limit the scope thereof.

CLAIMS:

1. A surgical kit or assembly for improving cardiac function, comprising:

an implantable scaffold or valve support device, said scaffold or valve support device defining an orifice, a prosthetic or bio-prosthetic valve being seatable in said orifice; and

fastening elements configured for attaching said scaffold or valve support device either (1) to heart or blood vessel tissue adjacent to a native heart valve, (2) at least indirectly to leaflets of a native valve of a patient, or (3) to both adjacent tissue and directly or indirectly to heart valve tissue, so that said scaffold or valve support device potentially is in effective force-transmitting and effective perivalvular fluid-sealing contact with said native valve and substantially fixedly attached to the patient.

2. The surgical kit or assembly of claim 1 wherein said scaffold or valve support device is insertable through a catheter, further comprising a multiplicity of tethers or suspension elements extending through said catheter, said tethers or suspension elements being adapted to position said scaffold or valve support device in apposition to said native valve

3. The surgical kit or assembly of claim 2 wherein said fasteners include one or more coupling elements with distal ends configured for attachment to said leaflets, said one or more coupling elements being coupled to said scaffold or valve support device, said tethers or suspension elements and said one or more coupling elements being adapted for moving said scaffold or valve support member on the one hand and said leaflets on the other hand towards one another.

4. The surgical kit or assembly of claim 3 wherein said tethers or suspension elements comprise one or more sleeves that surround respective ones of said one or more coupling elements and that extend through said catheter to said scaffold or valve support member, said sleeves and said coupling elements being movable relative to one another.

5. The surgical kit or assembly of claim 3 wherein each of said one or more coupling elements has a proximal end portion and a distal end portion, one of said proximal end portion and said distal end portion of each of said one or more coupling elements being separable from said scaffold or valve support device and from the respective other of said proximal end portion and said distal end portion, whereby said one of said proximal end portion and said distal end portion of each of said one or more coupling elements is removable from the patient after coupling of said scaffold or valve support device and indirectly said prosthetic or bio-prosthetic valve to said leaflets or subvalvular structures, the

other of said proximal end portion and said distal end portion of each of said one or more coupling elements being configured to remain affixed to said scaffold or valve support device and said leaflets or subvalvular structures.

6. The surgical kit or assembly of claim 2, further wherein said tethers or suspension elements are separably or releasably connected to said scaffold or valve support device.

7. The surgical kit or assembly of claim 1 wherein said scaffold or valve support device carries at least one closure member configured to effectuate closure of a gap between said leaflets and thereby at least reduce peri-valvular leakage.

8. The surgical kit or assembly of claim 7 wherein said at least one closure member is taken from the group comprising tissue approximation clip or anchor and a balloon.

9. The surgical kit or assembly of claim 1 wherein said scaffold or support device is provided with one or more tensile coupling elements having free ends attachable to a cardio-vascular wall or heart proximate said native valve.

10. The surgical kit or assembly of said 9, further comprising one or more tethers or elongate positioning members attached to said tensile coupling elements to position said ends of said one or more tensile coupling elements relative to said cardio-vascular wall or heart.

11. The surgical kit or assembly of claim 1 wherein said fastening elements are configured in part for operatively securing said scaffold of valve support device at least indirectly to chordae tendineae of the patient's heart.

12. The surgical kit or assembly of claim 1, further comprising an incremental advancement device to prevent moving of said scaffold or valve support device away from said native valve during the coupling of said scaffold or valve support device and indirectly said prosthetic or bio-prosthetic valve to said leaflets.

13. The surgical kit or assembly of claim 1 wherein said fasteners include a plurality of affixation tension members attachable to said leaflets or subvalvular structures.

14. The surgical kit or assembly of claim 1 wherein said scaffold or valve support device is insertable through a catheter and is connected to a multiplicity of tethers or

suspension elements, said fastening elements including a plurality of fixation devices or fastening elements slidable over or along said tethers or suspension elements into respective positions mutually spaced about a margin of said scaffold or valve support device, said tethers or suspension elements being removably attached to said scaffold or valve support device.

15. The surgical kit or assembly of claim 1, further comprising a capture device insertable though said native valve to capture a native leaflet, said capture device being configured to catch and entrain such leaflet or subvalvular structure.

16. An implantable device for use in valve placement in a subject, the device comprising:

a main body member defining an orifice for receiving or seating a prosthetic or bio-prosthetic valve; and

at least one fastener connected at least indirectly to said main body member for attaching said annular member to leaflets of a native valve.

17. The device of claim 16 wherein said at least one fastener includes one or more tensile coupling elements connected to said main body member for attaching same to the leaflets of said native valve, each said coupling element having a distal end with a hook, clip, barb, or other entrainment component for puncturing, capturing, or otherwise attaching to a valve leaflet or subvalvular structure of a native valve, said coupling components being disposed at intervals around a circumference of said orifice, said coupling elements being configurable to attach said main body member to the valve leaflets of said native valve so that said main body member is in fluid-tight contact with said valve leaflets and substantially fixedly attached thereto, further comprising a system of tether elements removably connected to said main body member for manipulating, positioning, and fixating of said main body member to the native valve.

18. The device of claim 17, further comprising at least one leakage-control element for closing a gap between adjacent ones of said valve leaflets, thereby at least reducing peri-valvular leakage, if necessary.

19. The device of claim 18 wherein said at least one leakage-control element is taken from the group consisting of (a) a flexible expandable member mounted to said main body member and an inflation tube connected to said expandable member for delivering a fluid thereto and (b) an approximation clip.

20. The device of claim 17 wherein said coupling elements are distal end portions of respective elongate tensile members having proximal end portions removably coupled to said distal end portions.

21. The device of claim 20, wherein said tether elements are in the form of elongate tubular members or sleeves each surrounding a respective one of said proximal end portions and in operative or effective engagement at a distal end with said main body member for pushing said main body member in a distal direction relative to said distal end portions of said tensile members, whereby said main body member is movable into engagement with the valve leaflets of said native valve.

22. The device of claim 17, further comprising a plurality of flexible elongate suspension elements connected to said main body member at intervals along a circumference thereof for attaching said main body member to a cardio-vascular wall proximate to said native valve.

23. The device of claim 22, wherein said tether elements are primary tether elements, further comprising a plurality of secondary tether elements extending to distal or free ends of said suspension elements for positioning said distal or free ends and fixing said distal or free ends to a cardio-vascular wall proximate to said native valve.

24. The device of claim 23 wherein:

said secondary tether elements can each be used to deliver a fastener which contains an orifice allowing the fastener to be advanced over or around the respective one of said secondary tether elements; and

each said secondary tether element being provided with a surrounding sleeve, or other advanceable component, slidably movable relative to the respective secondary tether element for advancing the respective said fastener,

distal ends of said secondary tether elements being removably attached to said distal or free ends of said suspension elements.

25. The device of claim 17 wherein said coupling elements are movably attached to said main body member initially for motion alternately in a distal direction and a proximal direction relative to said main body member.

26. The device of claim 25 wherein said coupling elements and said main body member are provided with cooperating ratchet components for preventing the hooks, barbs,

or other entrainment components at the distal ends of said coupling elements from moving away from said main body member once said main body member is advanced a predetermined distance over said coupling elements towards the hooks, barbs, or other entrainment components, whereby said main body member is locked into position and cannot be separated from said valve leaflets upon engagement of said main body member with the valve leaflets.

27. The device of claim 25 wherein said tether elements are tubular and coaxially surround proximal end portions of said coupling elements, said tether elements being incrementally advanceable in concert with a proximally directed retraction force exertable on said coupling elements, to induce said main body member and captured native valve leaflets to move towards and into contact with each other.

28. The device of claim 16 wherein said main body member has an outer margin, further comprising:

a plurality of tethers or support members each attached at distal or free ends to said margin, said tethers or support members being spaced from one another about said margin; and

a plurality of fixation devices or fastener elements spaced from one another about said margin and associated with respective ones of said tethers or support members,

said fixation devices or fastener elements being configured for at least partial insertion into organic tissue to attach said margin of said main body to a heart chamber or vessel wall.

29. The device of claim 28 wherein said fixation devices or fastener elements are each provided with at least one prong and a cap or head, said prong extending from said cap or head, said cap of head being connected to the respective one of said tethers or support members.

30. The device of claim 29 wherein said fixation devices or fastener elements each include at least two prongs or legs extending from the respective cap or head.

31. The device of claim 30 wherein said prongs or legs are helical.

32. The device of claim 29 wherein said fixation devices or fastener elements are movable over or along said respective ones of said tethers or support members into respective positions about said margin.

33. The device of claim 29 wherein said fixation devices or fastener elements are removably attached to said respective ones of said tethers or support members.

34. The device of claim 28 wherein said cap or head is provided with an orifice traversed by the respective one of said tethers or support members.

35. The device of claim 28 wherein said fixation devices or fastener elements are movable over or along said respective ones of said tethers or support members into respective positions about said margin.

36. The device of claim 28 wherein said fixation devices or fastener elements are removably attached to said respective ones of said tethers or support members.

37. The device of claim 28 wherein said respective ones of said tethers or support members are provided with sleeves engageable with the respective ones of said fixation devices or fastener elements for pushing same into organic tissue of a patient.

38. The device of claim 28 wherein said fixation devices or fastener elements each include a double helix element for penetrating a heart or blood vessel wall, said fixation devices or fastener elements each including a cap or head element configured for straddling a portion of said body member.

39. The device of claim 28 wherein said fixation devices or fastener elements are each provided with an orifice or lumen traversed by the respective one of said tethers or support members, whereby said fixation devices or fastener elements are slidable on said respective ones of said tethers or support members to come into contact with the heart or blood vessel wall at said margin.

40. The device of claim 28 wherein said fixation devices or fastener elements each include a catch element taken from the group consisting of a pin and a spring-loaded barb, for inhibiting unintended dislodgement of said fixation devices or fastener elements from said heart chamber or vessel wall.

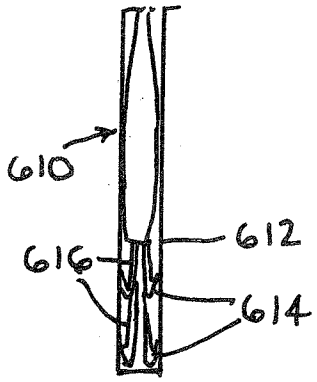


FIG. 1

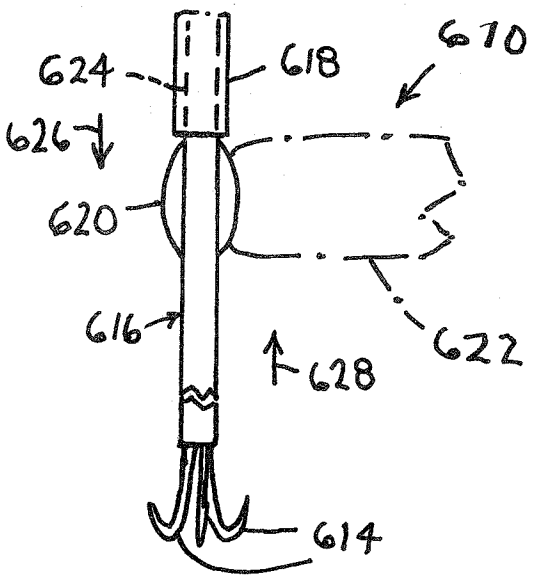


FIG. 2

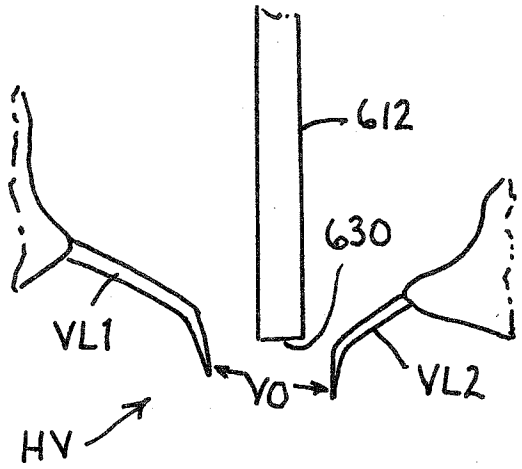


FIG. 3

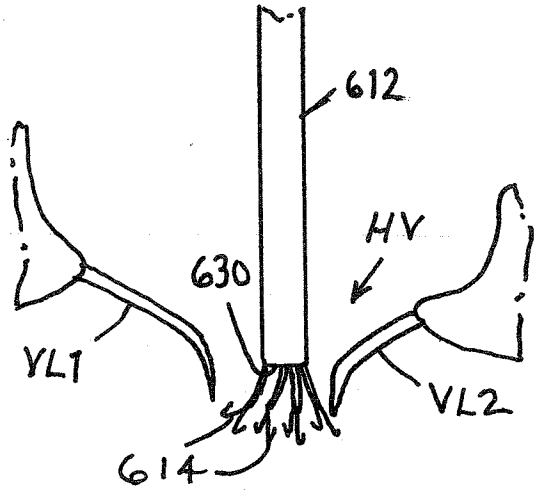


FIG. 4

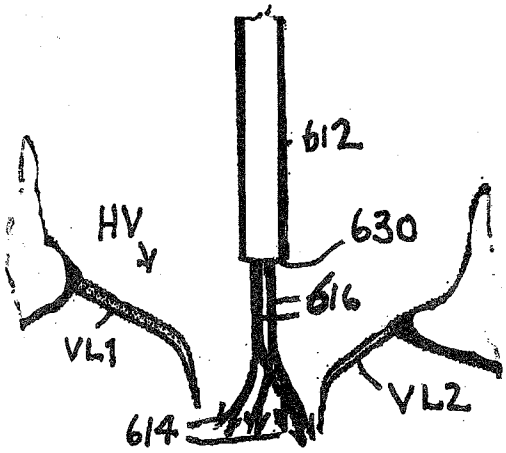


FIG. 5

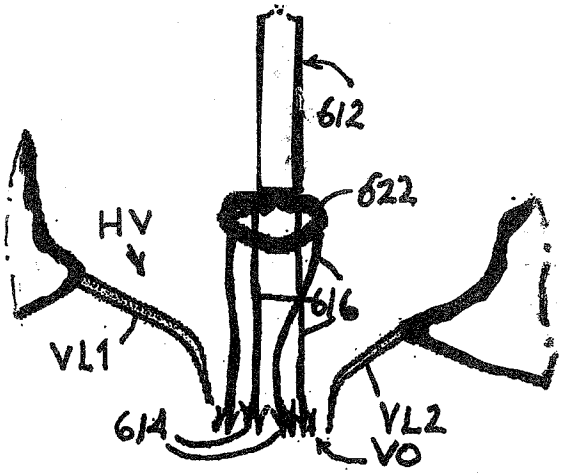


FIG. 6

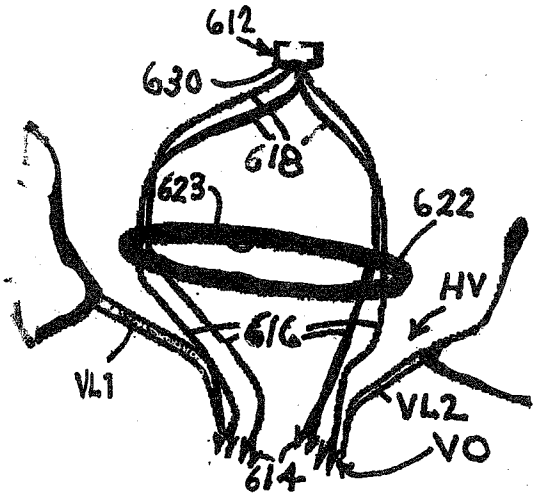


FIG. 7

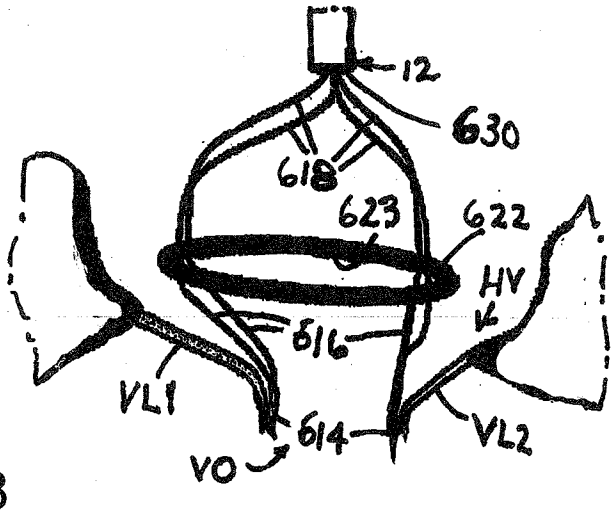


FIG. 8

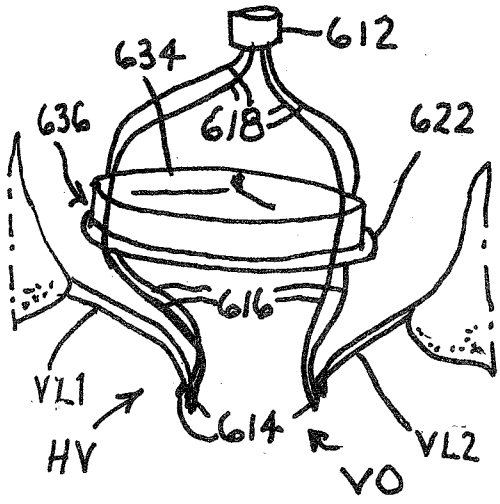


FIG. 9

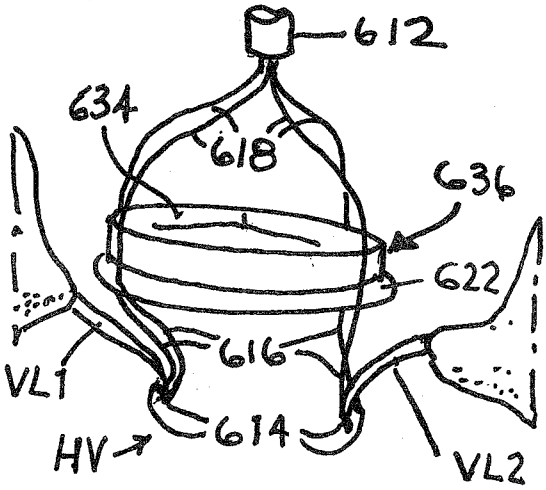


FIG. 10

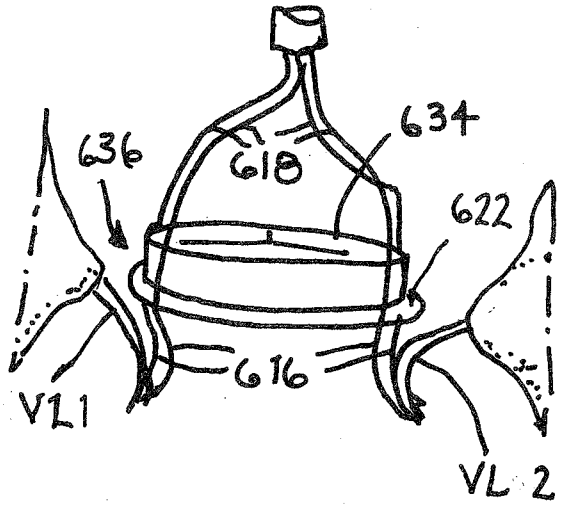


FIG. 11

FIG. 12

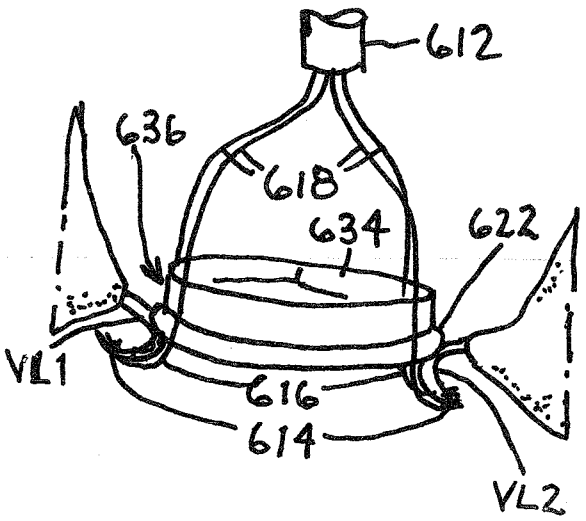
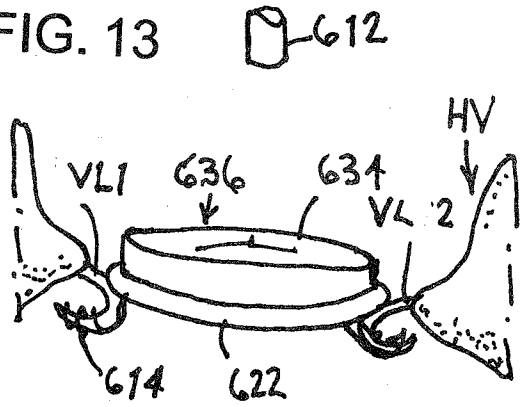


FIG. 13



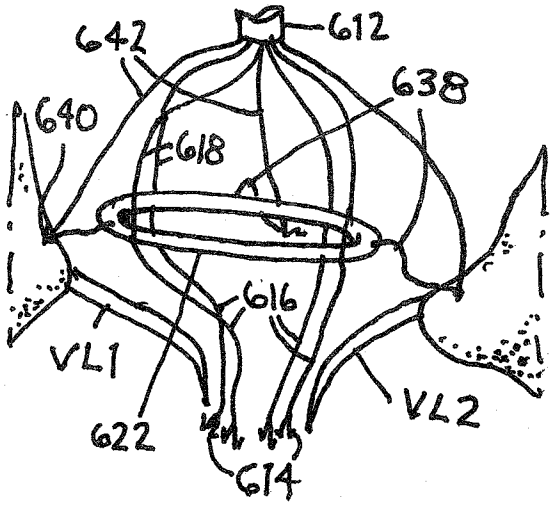


FIG. 14

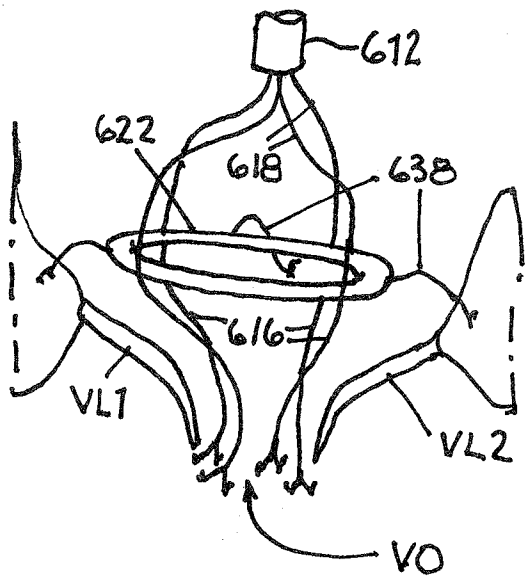


FIG. 15

FIG. 16

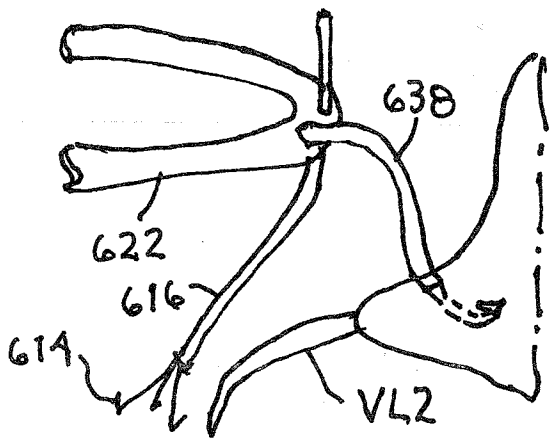


FIG. 17

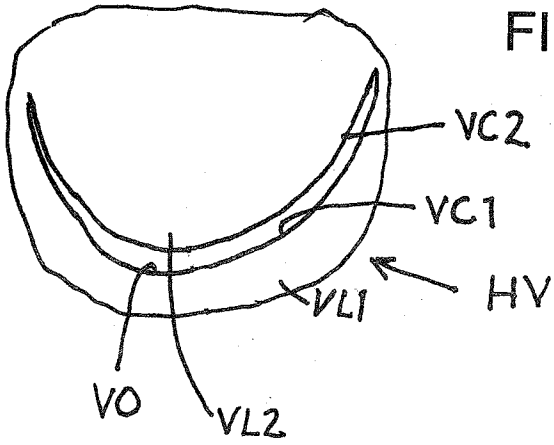
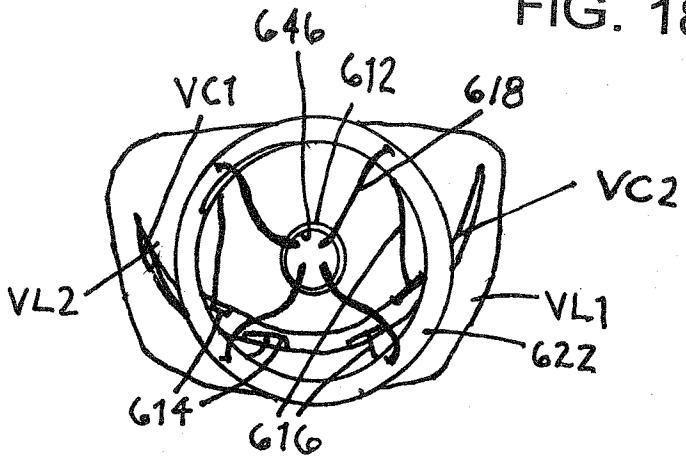


FIG. 18



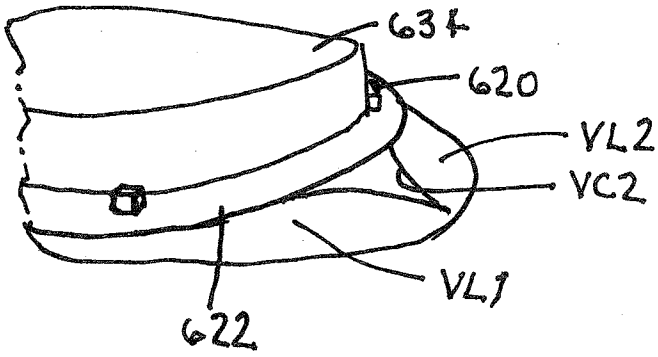


FIG. 20

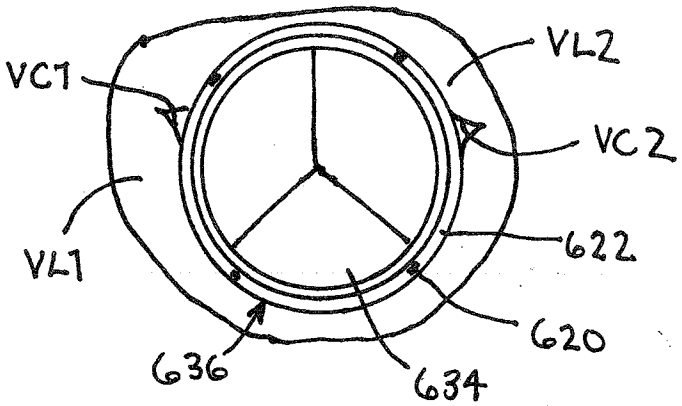


FIG. 19

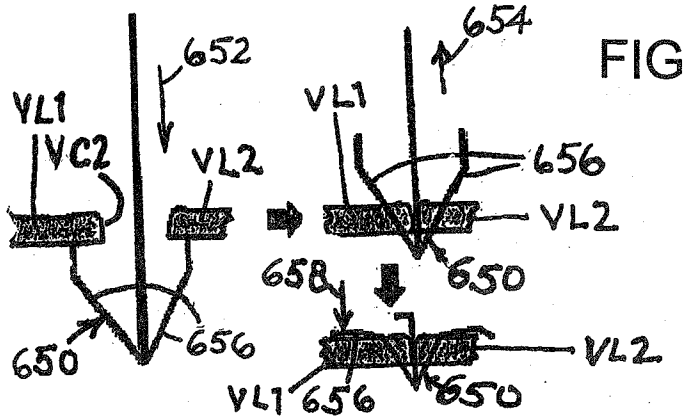


FIG. 21

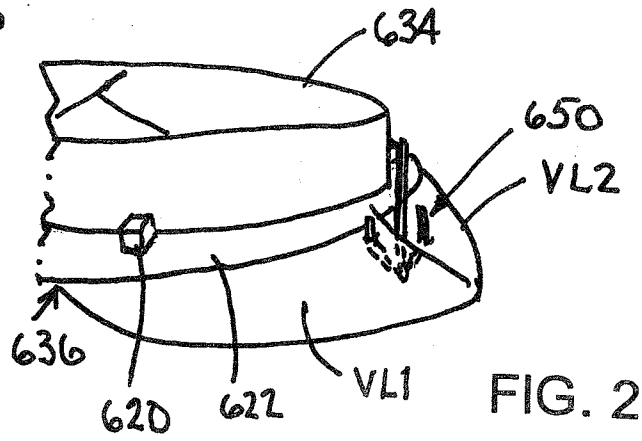


FIG. 22

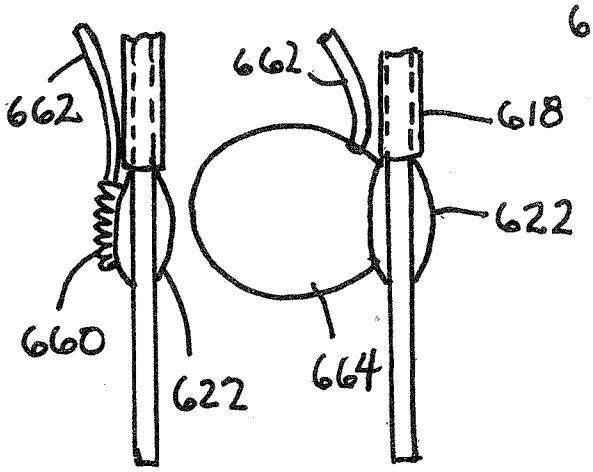


FIG. 23A FIG. 23B

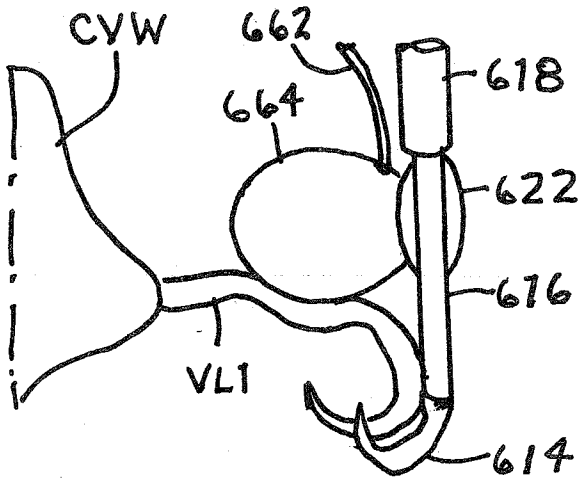


FIG. 24

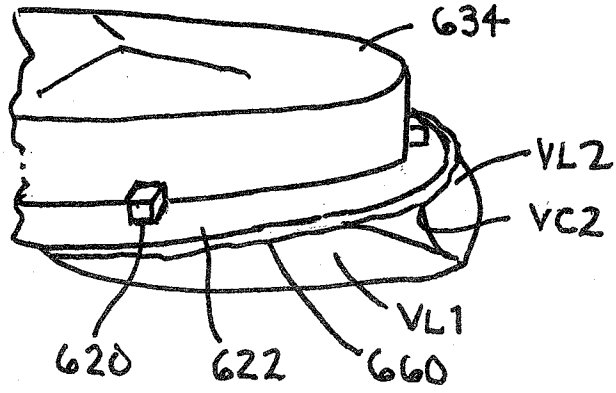


FIG. 25

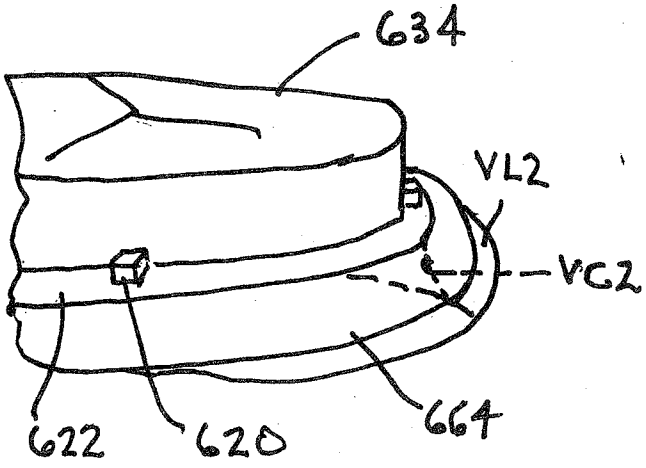


FIG. 26

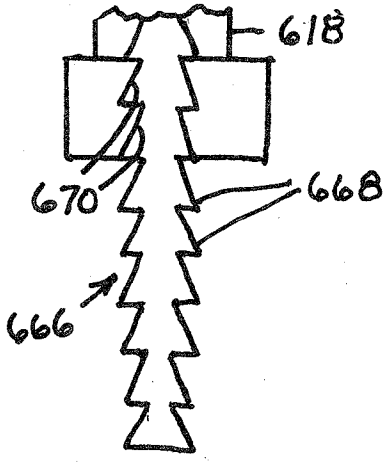
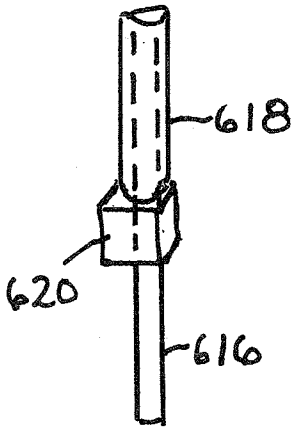


FIG. 27



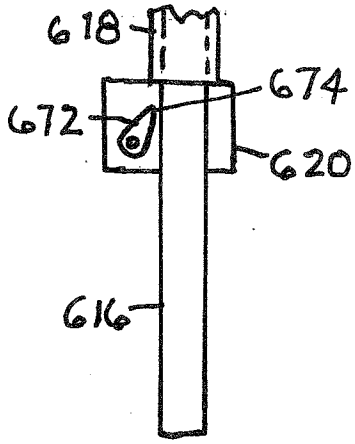


FIG. 28B

FIG. 28A

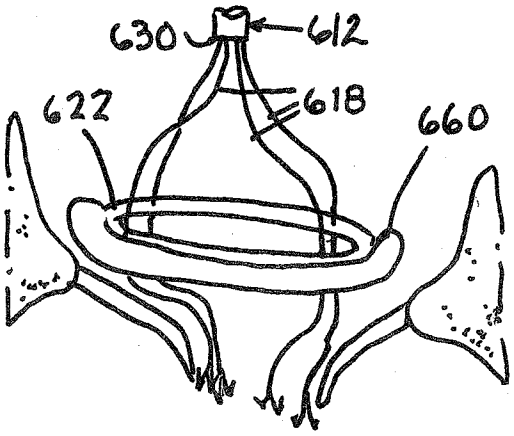


FIG. 29

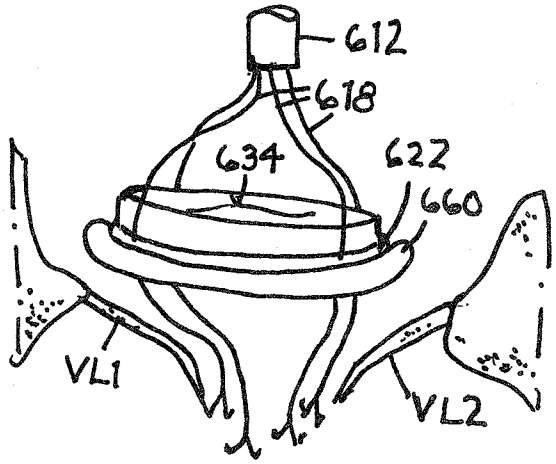


FIG. 30

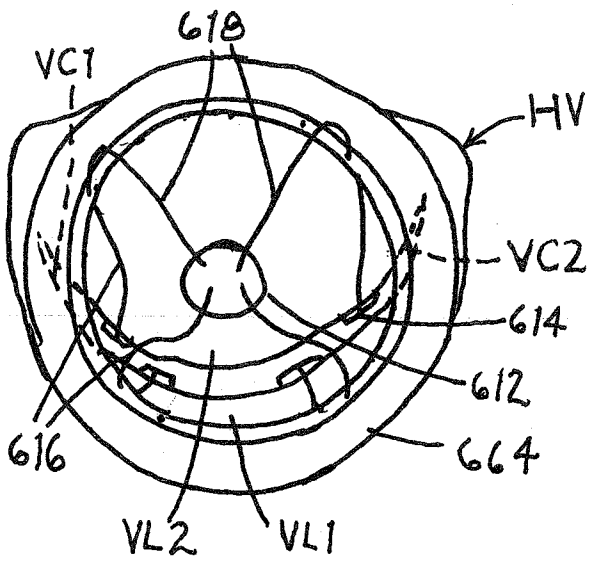


FIG. 31

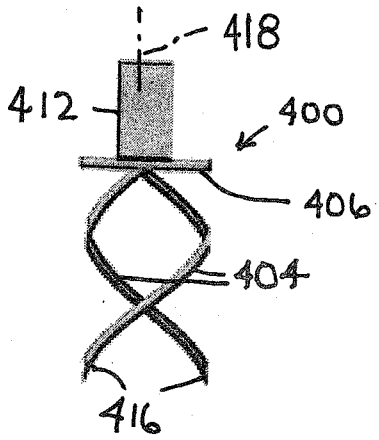


FIG. 32

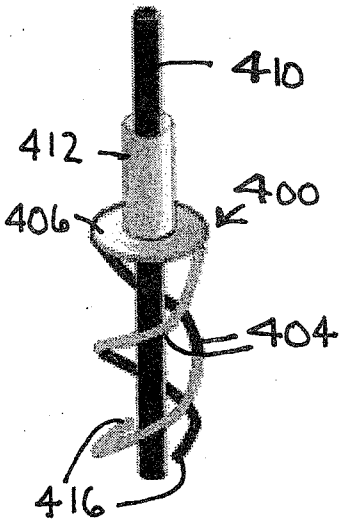


FIG. 33

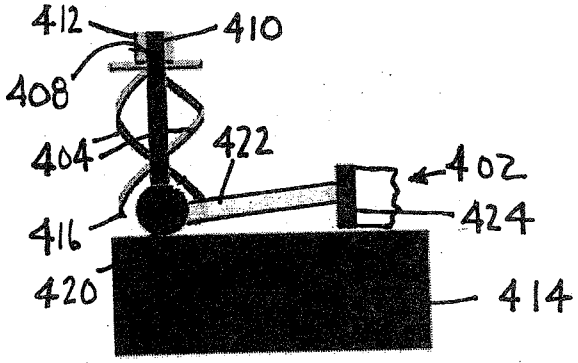


FIG. 34

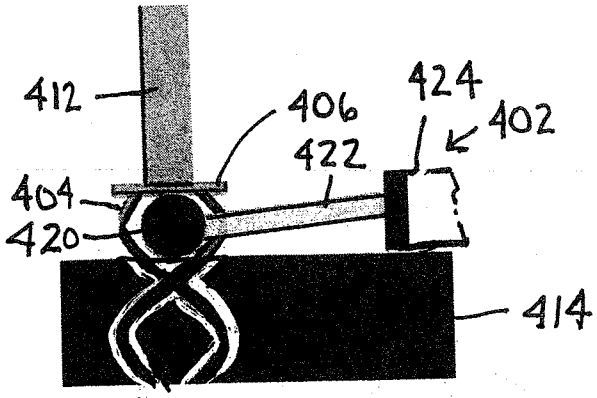


FIG. 35

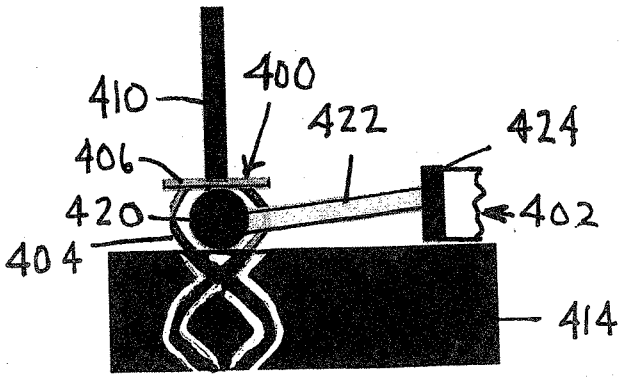
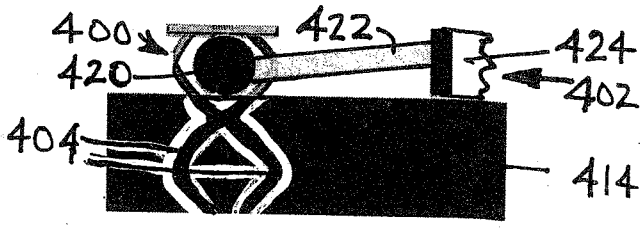


FIG. 36

FIG. 37



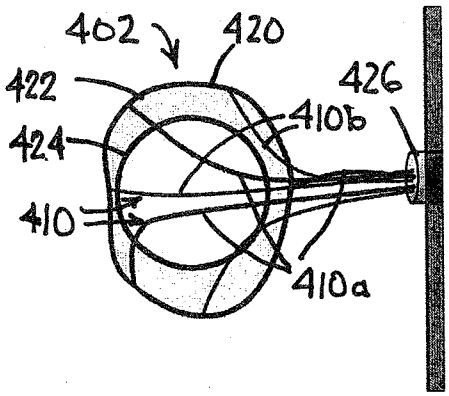
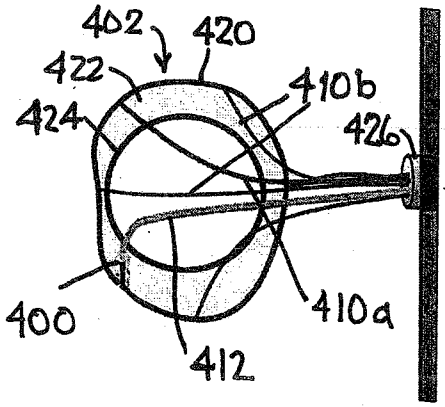


FIG. 38

FIG. 39



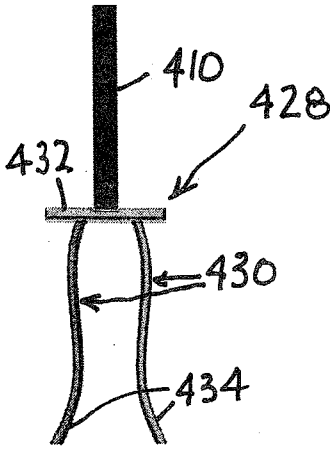


FIG. 40

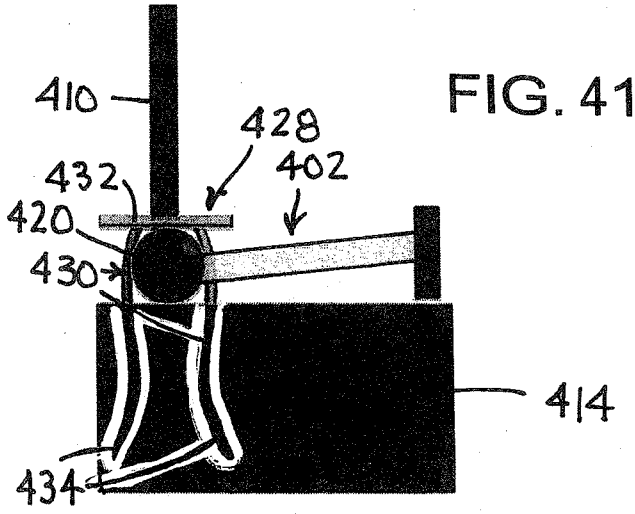


FIG. 41

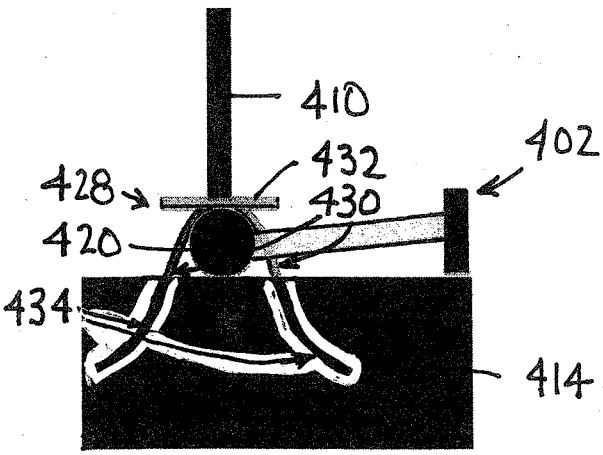


FIG. 42

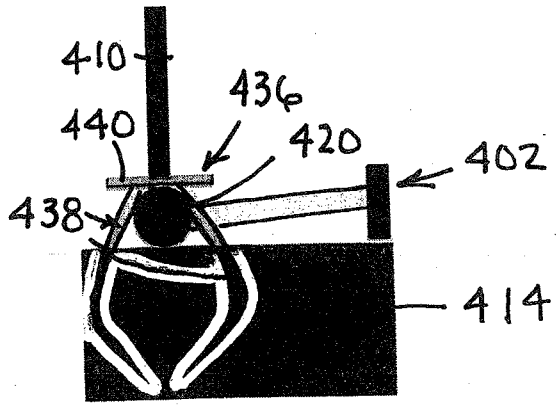


FIG. 43

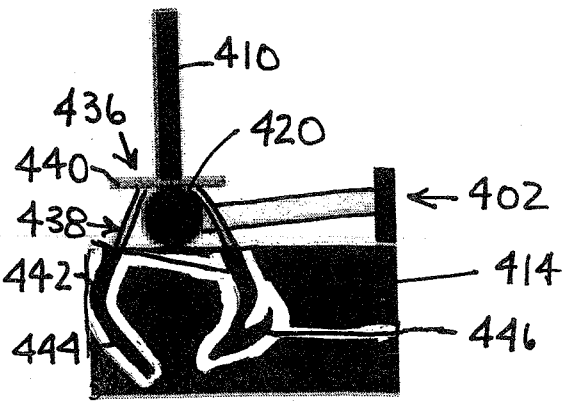


FIG. 44

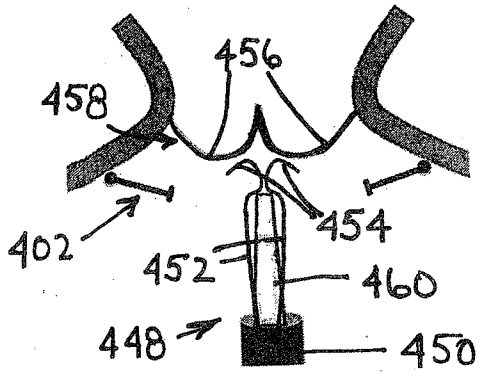


FIG. 45

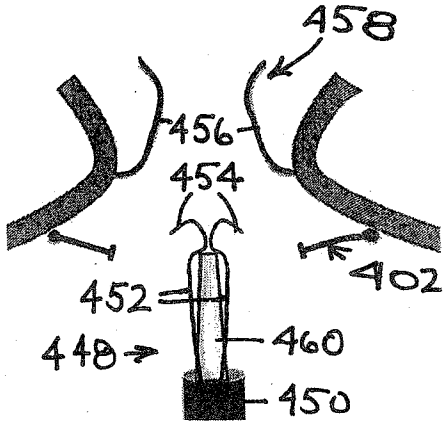


FIG. 46

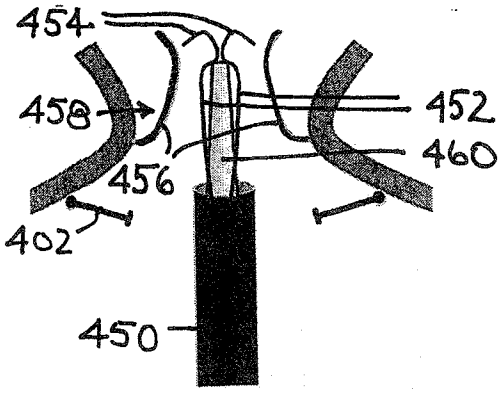


FIG. 47

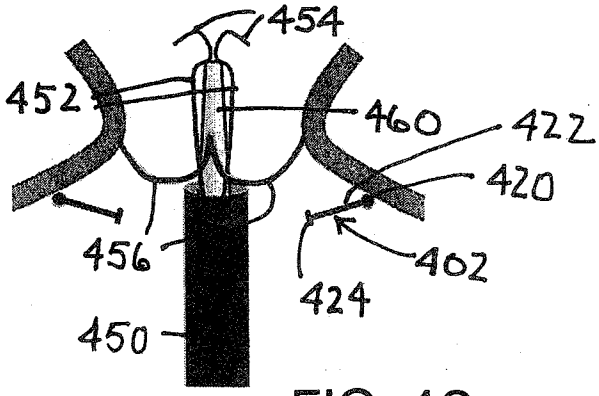


FIG. 48

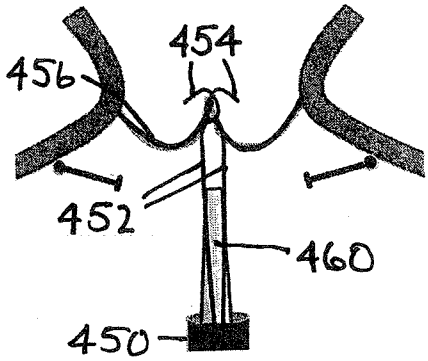


FIG. 49

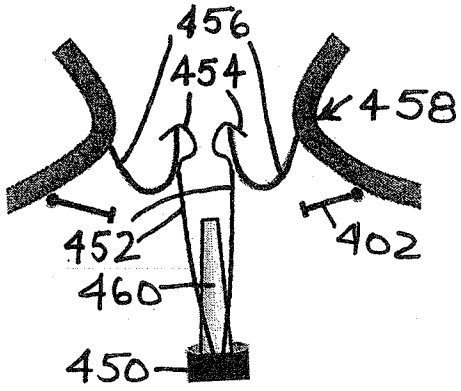


FIG. 50

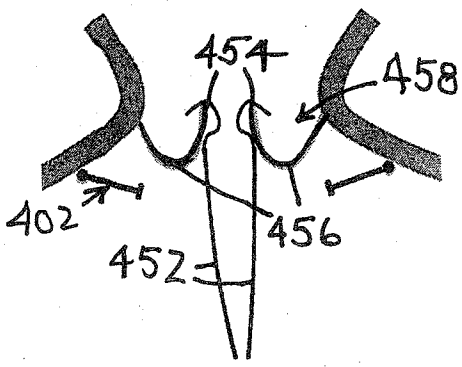


FIG. 51

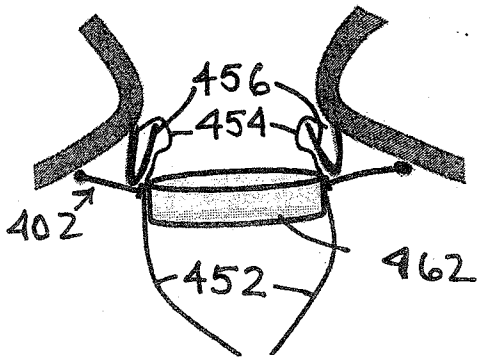


FIG. 52

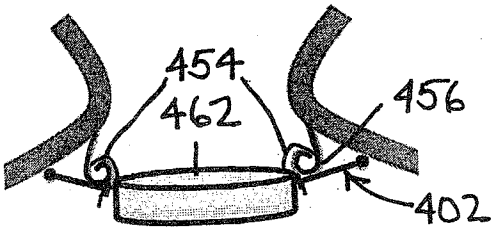


FIG. 53

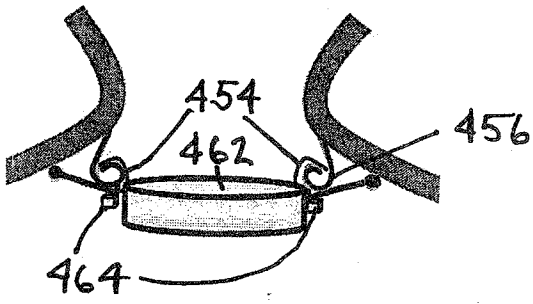


FIG. 54

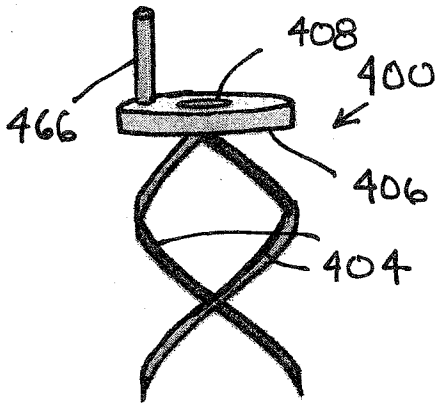


FIG. 55

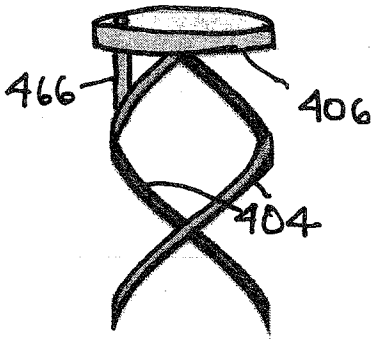


FIG. 56

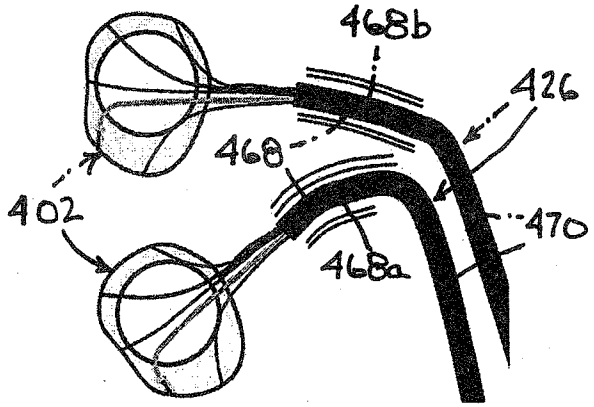


FIG. 57

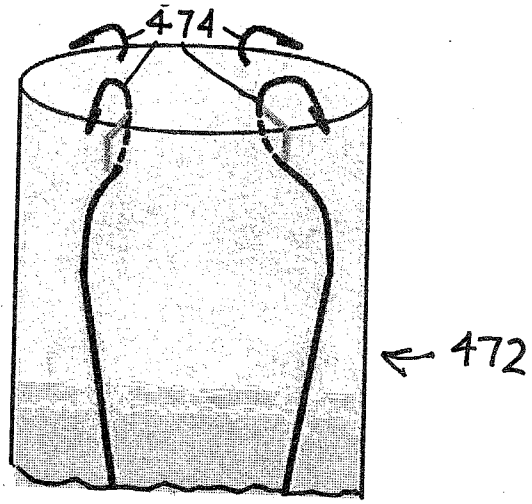


FIG. 58

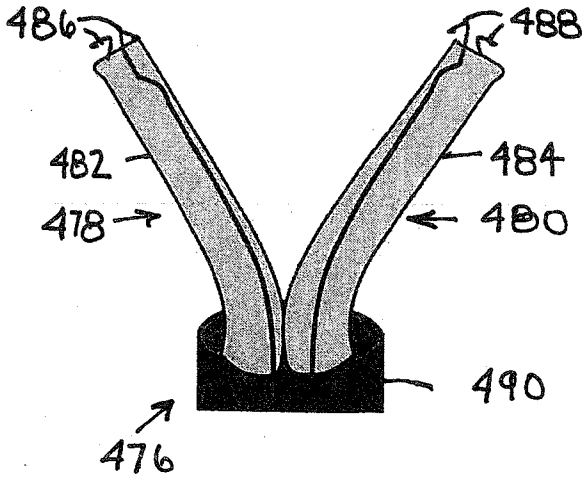


FIG. 59

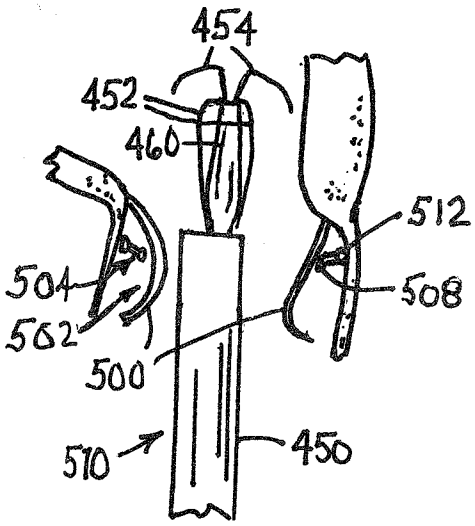


FIG. 60

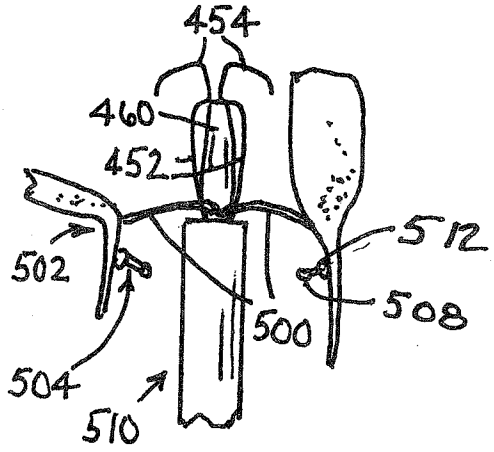


FIG. 61

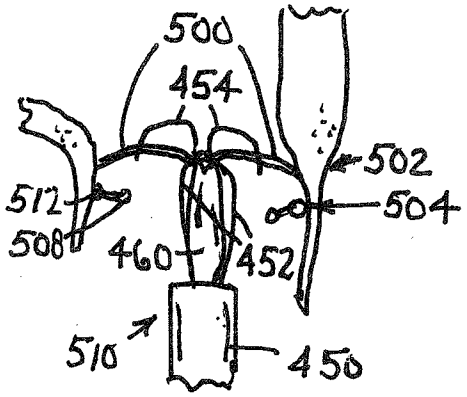


FIG. 62

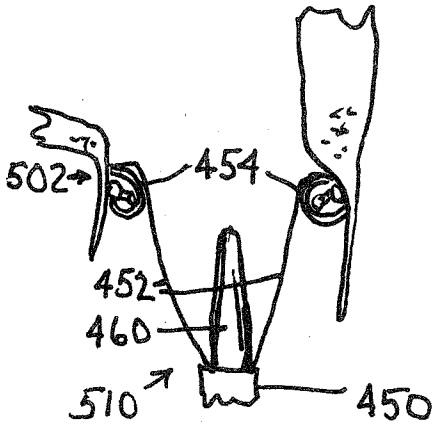


FIG. 63

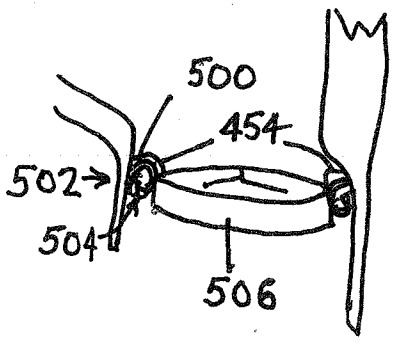


FIG. 64