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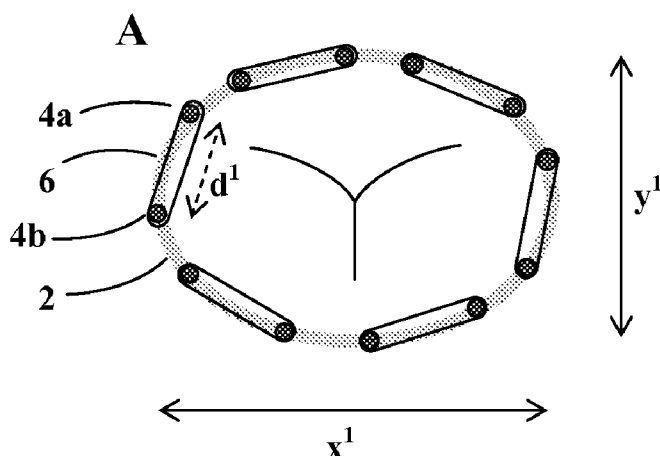
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- (54) Title: TREATMENT OF MITRAL REGURGITATION

FIG. 2

(57) **Abstract:** Provided are minimally invasive methods and kits for reducing a luminal dimension of the mitral annulus of a subject, in order to address mitral regurgitation in the subject. At least one pair of anchor posts are affixed to respective locations on the mitral annulus and drawn together by a tensioner that is drawn between the posts. The length of the annular tissue between the posts is shortened commensurate with the decrease in distance between the posts as a result of tensioning. The vector sum of the tensioned anchor pair or pairs provides at least one reduced luminal dimension.

TREATMENT OF MITRAL REGURGITATION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of U.S. Provisional App. No. 61/620,158, filed April 4, 2012, the entire contents of each of which are incorporated herein by reference.

TECHNICAL FIELD

[0002] The present disclosure relates to techniques and devices for alleviating mitral regurgitation.

BACKGROUND

[0003] Mitral regurgitation is characterized by failure of the mitral valve to close properly, leading to leakage of blood from the left ventricle, through the mitral valve, and into the left atrium when the left ventricle contracts. The most common type of heart valve insufficiency among the approximately 1.4 million people with heart valve disease, mitral regurgitation results in hundreds of thousands of hospital admissions and traditionally requires surgical repair or replacement in more than 50,000 people in the United States annually.

[0004] While numerous techniques presently exist for replacement or repair of the mitral valve, for example, via open-heart surgery, significant morbidity and mortality are still associated with surgical intervention. For this reason, a number of companies are working to develop percutaneous and otherwise minimally invasive approaches for treating mitral regurgitation.

[0005] One approach involves the investigational apposition of the mitral leaflets at their middle portion using a transeptally delivered clip. The MitraClip®, produced by Abbott Laboratories (Abbott Park, Illinois, U.S.A.) is said to have demonstrated certain clinical benefits for patients with “significant” mitral regurgitation, including improvements in heart function, quality of life, and normal physical activity, and a decrease in cardiac symptoms. A further experimental approach, developed by Endo valve, Inc. (Princeton, New Jersey), involves minimally invasive mitral valve replacement using a foldable prosthesis.

[0006] Despite such approaches, a need exists among patients with mitral regurgitation for additional, minimally invasive techniques for correcting mitral valvular defects, including among either higher-risk surgical patients or patients having milder cases of mitral regurgitation that are not candidates for open-heart surgery but would benefit from reparative intervention. A

technique with comparable or higher efficacy than existing measures would have profound medical implications both for those newly in need of valve repair, and among patients that are currently treated using alternative measures.

SUMMARY

[0007] The present disclosure provides methods and kits for use in the reduction of a luminal dimension of the mitral valve annulus of a subject. The methodologies and materials of the present disclosure may be employed via minimally invasive, percutaneous access to the atrial and/or ventricular spaces, thereby representing an advantageous approach for minimizing mitral regurgitation as compared with conventional techniques that may require open-heart surgery. Furthermore, while other, less invasive alternatives to open-heart access to the mitral valve do exist, the present disclosure provides a new variation for modulating the conditions that lead to mitral regurgitation that is readily integrated with existing systems and may be employed on an outpatient basis. Whereas the use of an undersized ring annulus implant (*see, e.g., Votta E, et al., ASAIO J. 2010 Nov-Dec;56(6):491-6*), radiofrequency or heat energy for shrinking annular collagen (*see, e.g., Goel R, et al., Catheter Cardiovasc Interv. 2009 Jul 1;74(1):43-8*), wires (*e.g., Mitralign, Inc., Tewksbury, MA*), or suturing have been proposed for correcting mitral regurgitation, these measures have met with limited success, and the presently disclosed technology represents an approach that permits the efficacious reduction of a luminal dimension of the mitral valve annulus that may be tailored in accordance with individual patient requirements.

[0008] Disclosed are methods for reducing a luminal dimension of a mitral valve annulus of a subject comprising affixing a first anchor post onto a first location on the annulus, affixing a second anchor post onto a second location on the annulus, the second location being an initial distance from the first location, and the first and second anchor posts collectively representing an anchor pair, tensioning the first anchor post and the second anchor post using a tensioner that is stretched between the first and second anchor posts in order to give rise to a resulting distance between the first location and the second location, the resulting distance being less than the initial distance.

[0009] Also disclosed are kits for use in reducing a luminal dimension of a mitral valve annulus of a subject comprising a steerable catheter comprising a proximal end and a distal end, the proximal end being operably associated with a steering mechanism, a plurality of anchor pairs respectively comprising first and second anchor posts, the distal end of the catheter being configured for housing an anchor pair and for affixing an anchor pair onto the annulus; and, a

material for tensioning the first and second anchor posts of each respective anchor pair when the first and second anchor posts are affixed onto the annulus.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. 1 shows how first and second anchor locations may be positioned relative to one another on the mitral annulus.

[0011] FIG. 2 illustrates an effect of affixing a series of anchor pairs onto a mitral valve annulus and using a tensioner that is stretched between the members of each respective pair.

[0012] FIG. 3 depicts a catheter in accordance with the present invention.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0013] The present inventions may be understood more readily by reference to the following detailed description taken in connection with the accompanying figures and examples, which form a part of this disclosure. It is to be understood that these inventions are not limited to the specific products, methods, conditions or parameters described and/or shown herein, and that the terminology used herein is for the purpose of describing particular embodiments by way of example only and is not intended to be limiting of the claimed inventions.

[0014] In the present disclosure the singular forms “a,” “an,” and “the” include the plural reference, and reference to a particular numerical value includes at least that particular value, unless the context clearly indicates otherwise. Thus, for example, a reference to “a material” is a reference to one or more of such materials and equivalents thereof known to those skilled in the art, and so forth. When values are expressed as approximations, by use of the antecedent “about,” it will be understood that the particular value forms another embodiment. As used herein, “about X” (where X is a numerical value) preferably refers to $\pm 10\%$ of the recited value, inclusive. For example, the phrase “about 8” preferably refers to a value of 7.2 to 8.8, inclusive; as another example, the phrase “about 8%” preferably (but not always) refers to a value of 7.2% to 8.8%, inclusive. Where present, all ranges are inclusive and combinable. For example, when a range of “1 to 5” is recited, the recited range should be construed as including ranges “1 to 4”, “1 to 3”, “1-2”, “1-2 & 4-5”, “1-3 & 5”, “2-5”, and the like. In addition, when a list of alternatives is positively provided, such listing can be interpreted to mean that any of the alternatives may be excluded, *e.g.*, by a negative limitation in the claims. For example, when a range of “1 to 5” is recited, the recited range may be construed as including situations whereby any of 1, 2, 3, 4, or 5 are negatively excluded; thus, a recitation of “1 to 5” may be construed as “1 and 3-5, but not 2”, or simply “wherein 2 is not included.” It is intended that any component,

element, attribute, or step that is positively recited herein may be explicitly excluded in the claims, whether such components, elements, attributes, or steps are listed as alternatives or whether they are recited in isolation.

[0015] Unless otherwise specified, any component, element, attribute, or step that is disclosed with respect to one embodiment of the present methods, products, systems, or kits may apply to any other method, product, system, or kit that is disclosed herein.

[0016] The disclosures of each patent, patent application, and publication cited or described in this document are hereby incorporated herein by reference, in their entirety.

[0017] It is known that providing an overall reduction in the luminal circumference of the mitral annulus can be effective to alleviate mitral regurgitation by, for example, drawing the mitral valve leaflets closer together. However, no existing strategy for reducing the luminal circumference is accepted among surgeons as representing a universal solution to the problem of mitral regurgitation, and additional alternatives remain of interest. Furthermore, presently available techniques cannot be tailored to provide efficacious reduction of a specific, desired luminal dimension of the mitral valve annulus. The present methods and kits fulfill the ongoing need for minimally invasive techniques for the reduction of the luminal circumference of the mitral valve annulus, and additionally permit the reduction of any desired luminal dimension, as dictated by the needs of a particular patient.

[0018] To this end and others, provided are methods for reducing a luminal dimension of a mitral valve annulus of a subject comprising affixing a first anchor post onto a first location on the annulus, affixing a second anchor post onto a second location on the annulus, the second location being an initial distance from the first location, and the first and second anchor posts collectively representing an anchor pair, tensioning the first anchor post and the second anchor post using a tensioner that is stretched between the first and second anchor posts in order to give rise to a resulting distance between the first location and the second location, the resulting distance being less than the initial distance.

[0019] Unlike many previous approaches, the present methods can effect the reduction of any dimension of the lumen that is defined by the mitral valve annulus. Certain patients may benefit from a reduction in the overall circumference of the lumen while substantially retaining the original configuration of the annulus. With respect to other patients, it may be desirable to reduce one dimension to a greater degree than another dimension; for example, the minor (septal-lateral) axis may be reduced to a greater degree than the major axis. In this way, any type of remodeling of the mitral annulus lumen may be provided. In addition, as described more fully herein, the present methods permit the practitioner to control the degree to which the selected

luminal dimension is reduced. For some patients a reduction in the luminal circumference of about 30% from its original state may be necessary to correct their particular case of mitral regurgitation, whereas other patients may only require a reduction of about 15-20%, while still other patients may require a reduction of up to 60% of a different luminal dimension. The present methods are compatible with adjustments of this variety and others from patient to patient.

[0020] In order to provide the reduction of a luminal dimension of the mitral annulus, at least one pair of anchor posts are affixed to the annulus and then drawn together by the application of tension. When the respective posts of a given pair are drawn together, thereby reducing the distance between the posts, the annular tissue between the posts (which are fixedly attached to the tissue at respective locations) is shortened to a commensurate degree. The posts may be made from any biocompatible material that is capable of being affixed to the annulus and is resilient enough to withstand the forces exerted when the respective posts of a given pair are tensioned. For example, the posts may be made from biocompatible metals (such as titanium, precious metals, or stainless steel), ceramics, synthetic polymers, natural polymers, any other material having the requisite characteristics, or any combination thereof. Those of ordinary skill in the art may readily identify other materials that are biocompatible and have the other desired characteristics for use in forming the posts, and any such material or combination of materials may be used.

[0021] The posts may be substantially elongated, *i.e.*, having a long axis and a short axis, such as in the nature of a peg, nail, needle, rivet, or like structure. Optionally one or both ends of the post may be tapered to improve the ability of the post to penetrate the annular tissue. One or both ends may also or alternatively be barbed, ridged, serrated, or otherwise textured to improve the ability of the post to remain in place within the annular tissue, to maintain contact between the post and the tensioner (*e.g.*, by providing a point or points of fixation for the tensioner on the post or by providing a high-friction surface to prevent the tensioner from slipping from its position on or in the post). In another example, the post is substantially elongated, one end being tapered for penetration into the annular tissue, and the other end bearing a cap in the nature of a head on a nail. In a further example, the post is substantially elongated, one end being barbed for improving fixation of the post in the annular tissue, the other end bearing a slit or eyelet that may be used to secure the tensioner to the post. A post may be solid or hollow. In one example, the post is tubular, with one end being open, the other end being closed or featuring a cap or head. Any combination of the above described options for the respective ends of the post may be used with respect to a given post. In other embodiments, the

post may resemble a tack. For example, the post may feature a wide head and a narrow spike that extends from the center of the head, or a series of spikes or barbs or other extensions, preferably tapered, from any portion of the head, such as the outer circumference. In still other embodiments, the post may approximate a staple. In any of the preceding embodiments, the post may feature a portion or end (or multiple portions or ends) that is substantially hook-shaped that can function to affix the post to the annular tissue. Any structure that may be delivered to the mitral valve annulus, affixed to the annulus, and tensioned while remaining affixed to the annulus may be used for the present posts.

[0022] The posts are sized in a manner that is consistent with a number of desired characteristics. For example, when adopting an elongated morphology, the posts are of sufficient length so that a when portion thereof is implanted into the annular tissue to the extent necessary to remain stable and in place during tensioning, a sufficient length of the post remains outside of the annular tissue for interaction with the tensioner. The width or gauge of the post should be sufficient to permit fixation onto or into the annular tissue without distorting the annulus or encroaching on any other local physiological feature or an adjacent post. The size of the posts should be such that, for example, as many as 24 posts (12 anchor pairs), 22 posts (11 anchor pairs), 20 posts (10 anchor pairs), 18 posts (nine anchor pairs), 16 posts (eight anchor pairs), 14 posts (seven anchor pairs), 12 posts (six anchor pairs), 10 posts (five anchor pairs), or 8 posts (four anchor pairs) can be affixed onto the mitral annulus while retaining the preferred characteristics recited above. In some embodiments, a post may be about 0.5 mm to about 5 mm long and have a thickness that is equivalent to a 20-gauge needle (0.902 mm) or smaller (*i.e.*, higher gauge).

[0023] The first and second posts of an anchor pair according to the present methods are respectively affixed to the annulus at an initial distance from one another. This distance is reduced when the posts are tensioned using a tensioner. The initial distance between the posts depends on the desired outcome of the tensioning. For example, if the desired outcome is to contract a contiguous portion of the mitral annulus, then the initial distance between the posts may be about 5 mm, about 6 mm, about 7 mm, about 8 mm, about 9 mm, about 10 mm, about 11 mm, about 12 mm, about 13 mm, about 14 mm, or about 15 mm. If the desired outcome is to shorten an axis of the lumen, for example, to shorten the septal-lateral axis, then the initial distance between the posts will be the length of the septal-lateral axis of the untreated subject.

[0024] The locations on the annulus to which the first and second anchor posts of a given anchor pair are affixed, *i.e.*, the first and second locations, respectively, may be anywhere on the mitral annulus. Both the first and second locations may be on the atrial side of the

annulus, or both the first and second locations may be on the ventricular side of the annulus. In some embodiments, the first location may be on one of the atrial side or the ventricular side of the annulus, and the second location may be on the other of the atrial side or the ventricular side of the annulus. The first location may be about 2 mm to about 50 mm from the second location. The first location may be adjacent to the second location on the annulus. Two locations are “adjacent” to one another when an imaginary line drawn between the two locations does not substantially cross an axis of the annulus; for example, given a first location on the annulus, a second location will be “adjacent” if it is about 20 mm or less around the circumference of the annulus from the first location. The first location on the annulus may be about 2 to about 20 mm from the second location on the annulus. For example, the first location may be about 2 mm, about 5 mm, about 6 mm, about 7 mm, about 8 mm, about 9 mm, about 10 mm, about 12 mm, about 15 mm, about 17 mm, or about 20 mm from the second location. In other embodiments, the first location may be substantially across an axis of the mitral annulus from the second location. For example, when the distance between two locations on the annulus is about 30 mm or more, the two locations will be across an axis of the mitral annulus, and not adjacent to one another. For example, the first location may be about 25 mm, about 30 mm, about 32 mm, about 34 mm, about 38 mm, about 40 mm, about 42 mm, about 44 mm, about 46 mm, about 48 mm, or about 50 mm from the second location. FIG. 1 depicts a first location (L_1) on mitral valve annulus 2 that may properly be termed adjacent to a second location (L_2). In contrast, first location L_1' is substantially across an axis of annulus 2 and not adjacent to second location L_2' (in this case, L_1' is substantially across the “minor” or septal-lateral axis from second location L_2').

[0025] The first and second posts of an anchor pair may be affixed simultaneously or separately. For example, if the first and second posts are to be affixed to adjacent portions of the annulus, then it may be desirable to affix the posts substantially simultaneously. On the other hand, if the first and second posts are to be affixed respective portions of the annulus that are on substantially the opposite sides of an annular axis (*e.g.*, the septal-lateral axis), then it may be desirable to affix one post prior to affixing the second post.

[0026] Any appropriate mode of affixing a post to the annulus may be used. In one embodiment, a post may be affixed to the annulus by propelling the post into the annulus. The means of propulsion may be fluid (*e.g.*, air or liquid) or mechanical. Mechanical propulsion includes, for example, stapling, riveting, staking, and the like. In certain embodiments, a post may be affixed to the annulus by use of an adhesive. Biocompatible adhesives are known among those skilled in the art, and any appropriate bioadhesive may be selected. In other embodiments, a post may be affixed to the annulus by hooking the post through the annular tissue, much like a

fishhook penetrates and anchors to tissue. Any of the preceding techniques or combination thereof may be used to affix a post to the mitral annulus.

[0027] The first and second posts of an anchor pair are tensioned using a tensioner that is stretched between said first and second anchor posts. In one embodiment, the tensioner is stretched between the respective posts of an anchor pair before one or both of the posts is affixed to the annulus. For example, the tensioner may be stretched between the respective posts of an anchor pair before either of the posts is affixed to the annulus. The tensioner may be any material or combination of materials that induces a force that draws the first and second posts of an anchor pair together. Any elastic, biocompatible material that is not bioresorbable (*i.e.*, does not break down except at a desired rate under normal physiological conditions at the mitral valve) would suit this purpose, nonlimiting examples of which include silicone, natural or synthetic rubber, polymers (*e.g.*, polyurethane-based polymers), or combinations thereof. The tensioner may be a substantially circular band or otherwise include circular or looped features that may be looped over respective anchor posts of an anchor pair. In other embodiments, the tensioner may be a length of material that is fixedly attached to each post, wherein any means of fixation may be used; one example is where a post contains an eyelet or slit and an end of the length of tensioner material is secured by tying thereto.

[0028] The tensioning of the first anchor post and the second anchor post of a given anchor pair using a tensioner gives rise to a resulting distance between the first location and the second location, the resulting distance being less than the initial distance. The resulting distance may be, for example, about 5% to about 60% less than the initial distance. In other words, the vector sum of the tension between the first anchor post and second anchor post draws the first and second posts together, and as the posts are affixed to respective locations on the annulus, the respective locations to which the posts are attached are also drawn together, thereby giving rise to a reduced luminal dimension of the annulus. Thus, by affixing first and second anchor posts to respective locations on a mitral annulus, and tensioning the posts using a tensioner that is stretched therebetween, a luminal dimension of the mitral annulus may be reduced.

[0029] Uniquely, the present methods permit the reduction of any luminal dimension of the mitral annulus by any desired amount. The present methods permit the practitioner to exert some control over the degree to which the initial distance between the first and second anchor posts of an anchor pair is reduced to provide the resulting distance. This may be accomplished by selecting the modulus of elasticity of the tensioner that is stretched between said first and second anchor posts. The modulus of elasticity depends on the type of material of which the tensioner is made, as well as the thickness of the tensioner. For example, a wider band of a given

material will have a higher modulus of elasticity than a narrower band of the same material. Thus, selection of the modulus of elasticity for the tensioner may include selection of a material for the tensioner, selection of the physical characteristics (*e.g.*, thickness, shape, *etc.*) of the tensioner, or both. Given the known physical characteristics of biocompatible materials that may be used to provide the tensioner, those of ordinary skill in the art may readily select a material and its characteristics in order to provide a desired modulus of elasticity, and in turn a desired degree to which the initial distance between the first and second anchor posts of an anchor pair is reduced to provide the resulting distance.

[0030] The present methods may further comprise affixing first and second anchor posts of a (*i.e.*, at least one) further anchor pair onto respective locations on the mitral annulus, and tensioning the first anchor post and the second anchor post of the further anchor pair. The instant methods may also comprise affixing first and second anchor posts of a plurality of further anchor pairs on the annulus, and tensioning the first anchor post and the second anchor post of each respective further anchor pair. Thus, at least one further anchor pair may be affixed to the mitral annulus under any of the conditions and using any of the parameters that are described above with respect to the initial anchor pair. The respective locations of the members of the further anchor pair or pairs are preferably different than the locations of anchor posts of any other anchor pair, although the locations of anchor posts of different anchor pairs may be adjacent to one another. FIG. 2A depicts a series of pairs of posts 4a, 4b that are affixed on to the mitral annulus 2 and tensioned with a tensioner 6. The view provided by FIGS. 4A and 4B is downward onto the atrial side of the mitral annulus 2. FIG. 2A shows an imaginary situation whereby each pair of posts 4a, 4b is tensioned with a tensioner 6, but the posts have not yet drawn together as a result of the tensioning; thus, mitral annulus 2 is shown in FIG. 2A as it would appear before the initial distance d^1 between posts 4a, 4b is decreased as a result of tensioning, *i.e.*, in its unaltered, natural state before treatment according to the present methods. At this time mitral annulus 2 has a minor axis with a length of y^1 and a major axis with a length of x^1 . FIG. 2B shows mitral annulus 2 as it would appear after the tensioning between each pair of posts 4a, 4b by tensioners 6 has caused each pair of posts 4a, 4b to be drawn together, such that the resulting distance d^2 between an exemplary pair of posts 4a, 4b is less than initial distance d^1 . In FIG. 2B, the vector sum of the tensioning between each pair of posts 4a, 4b has resulted in a decrease of the minor axis dimension to a resulting length of y^2 and decrease of the major axis dimension to a resulting length of x^2 . In addition, the annular circumference has been decreased from an initial circumference C^1 (*i.e.*, the circumference of annulus 2 shown in FIG. 2A) to a resulting circumference C^2 . Accordingly, FIG. 2 illustrates some exemplary effects of

affixing a series of anchor pairs onto a mitral valve annulus and tensioning the respective pairs using a tensioner that is stretched between the members of each respective pair, in accordance with the present methods.

[0031] The present methods may therefore be carried out such that vector sum of the tensioning between first and second members of respective anchor pairs gives rise to a reduced luminal dimension. The present methods may reduce the luminal circumference, the short (septal-lateral) annular dimension, the long annular dimension, or any other annular dimension. As described above, the degree of reduction of a luminal dimension may be controlled based on a number of factors. As a result, a given luminal dimension may be decreased in accordance with the present methods by about 1% up to about 60%. For example, a luminal dimension may be decreased by about 1%, about 5%, about 10%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, or about 60%. In some embodiments, the luminal circumference is decreased by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, or about 40%. In other embodiments, the septal-lateral axis of the lumen may be decreased by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, or about 60%. According to the needs of a particular patient, the practitioner may select a degree of reduction of a luminal dimension as desired.

[0032] The present disclosure also provides kits for use in reducing a luminal dimension of a mitral valve annulus of a subject comprising a steerable catheter comprising a proximal end and a distal end, the proximal end being operably attached to a steering mechanism, a plurality of anchor pairs respectively comprising first and second anchor posts, the distal end of the catheter being configured for housing an anchor pair and for affixing an anchor pair onto the annulus; and, a material for tensioning the first and second anchor posts of each respective anchor pair when the first and second anchor posts are affixed onto the annulus.

[0033] The catheter of the present system includes a distal end, which is the end of the catheter that is first introduced into the physiological point of entry during the procedure for reducing a luminal dimension of a mitral valve annulus. The proximal end of the catheter (defined herein as the end of the catheter that is closest to the operator of the system during use) remains outside of the subject. The instant catheters may have a length of about 20 cm to about 200 cm from the distal end to the proximal end. The outer diameter of the catheter may be, for example, about 0.5 cm to about 10 cm.

[0034] The catheter may be constructed from any suitable material, wherein suitability is determined by such considerations as biological compatibility, durability, the appropriate

balance between rigidity and flexibility, and other readily appreciable factors based on the intended use of the catheter. For example, polyimide, polyethylene, polypropylene, Kalrez®, Simriz®, Viton®, Chemraz®, silicone, neoprene, nitrile, metal or metal alloys (such as Ti-Nb-Zr; see, e.g., U.S. Pat. No. 5,685,306) or any other combination thereof may be used. The materials used for the construction of the catheter, as well as the methods for the construction thereof, are readily appreciated by those skilled in the art, and all appropriate materials and means of construction are contemplated herein.

[0035] The catheter may include at least one lumen. For example, the catheter may comprise two lumens, the first being a guidewire lumen to permit the catheter to be translated along a guidewire, the second being a steering lumen for accommodating a tension cable for steering the catheter. The guidewire lumen is appropriately sized, shaped, and located within the catheter to accommodate a guidewire, such that the catheter may be translated over a guidewire that has been placed along the appropriate physiological pathway to a site of interest within a subject. The steering lumen is appropriately sized, shaped, and located within the catheter to accommodate a tension cable. The manipulation of a tension cable that is located within a lumen of the present catheters causes the deflection of the catheter, which in turn allows the catheter to be moved from a first location to a second location in situ. The selection and use of guidewires and steering tension cables are well known among those skilled in the art. There are no limitations on the relative arrangement of the lumens within the catheter. However, it is traditional for a guidewire lumen to be located towards the center of a catheter. In one embodiment, the guidewire lumen and the steering lumen are provided in a side-by-side arrangement within the catheter. In other instances, the guidewire lumen may be located substantially in the center of the catheter, and the steering lumen is located between the guidewire lumen and the outer surface of the catheter. It may be desirable to include more than one steering lumen, wherein each steering lumen may accommodate a separate tension cable, in order to enhance the steerability of the catheter. For example, an exemplary catheter may include a single guidewire lumen and two, three, or four separate steering lumens.

[0036] The kits according to the present disclosure may further comprise a steering mechanism that is operably associated with the proximal end of the present catheters. For example, the steering mechanism may be operably associated with a tension cable or cables at the proximal end of the catheter, for deflecting the distal end of the catheter in at least one directional plane. In such instances, the association between the steering mechanism and the tension cable or cables is described as operable because the steering mechanism makes use of its connection to the tension cable to deflect the leading tip. The use of tension cables for the

deflection of a catheter is readily understood among those skilled in the art. The steering mechanism may be any device that allows a user to manipulate the tension cable(s) and thereby the catheter in the intended manner – for example, an obturator knob, lever, dial, or any appropriate mechanism may be used. The deflection of the distal end by use of the steering mechanism permits both the guidance of the catheter through a subject's vasculature (for example, to effect the downturn into the subject's ventricle) and the precision placement of the catheter at or near the site of implantation. The steering mechanism is typically used in conjunction with an appropriate imaging technology, such as fluoroscopy or echocardiography.

[0037] The present kits also comprise a plurality of anchor pairs respectively comprising first and second anchor posts. Also included in the present kits is a material for tensioning the first and second anchor posts of each respective anchor pair when the first and second anchor posts are affixed onto the annulus. Each of the attributes, components, materials, and the like that are described above with respect to the inventive methods (*e.g.*, concerning the anchor posts and the material for tensioning the first and second anchor posts of an anchor pair) may be used in accordance with the items that are included in the present kits. In some embodiments, the present kits may include at least about five anchor pairs and material for tensioning the posts of each of the anchor pairs. For each anchor pair that is provided in a kit, there should preferably be sufficient material for tensioning the respective anchor members of each pair. For example, there may be at least 24 posts (12 anchor pairs), 22 posts (11 anchor pairs), 20 posts (10 anchor pairs), 18 posts (nine anchor pairs), 16 posts (eight anchor pairs), 14 posts (seven anchor pairs), 12 posts (six anchor pairs), 10 posts (five anchor pairs), or 8 posts (four anchor pairs), and at least as much material as is necessary to tension the first and second members of each pair.

[0038] The catheters of the present kits are specially adapted for use in reducing a luminal dimension of a mitral valve annulus of a subject. For example, the catheters are configured for housing an anchor pair, and for affixing an anchor pair onto said annulus. FIG. 3A depicts a simplified illustration of an exemplary catheter 8 that houses a pair of anchors 4a, 4b at distal end 10. The “housing” of anchors by the catheter may comprise securely retaining the anchors until the catheter is positioned near a desired location on the annulus onto which an anchor may be affixed. An anchor may be housed within a specialized element of the catheter, for example, an appropriately sized lumen. In some embodiments, the anchors are housed within respective lumens of the catheter, wherein the lumens may be pressurized or equipped with mechanical drivers in order to propel the anchors from the respective lumens into the mitral annulus. The catheter may also be configured such that a given lumen for housing and deploying

an anchor may also be “reloaded” with a further anchor that can in turn be ejected from the lumen to the annulus when the catheter is repositioned as desired. Regardless of whether lumens or some other feature(s) are used to house the anchors, the catheter may be configured for affixing an anchor pair onto the annulus by propelling the first and second anchor posts into the annulus. The catheter may propel the anchors using any available means, including a pneumatic system (using pressurized fluid, *e.g.*, air or liquid to effect mechanical motion) or mechanically-induced propulsion. Other means for propelling the anchors will be readily appreciated, and the integration of such means into the present catheters is a matter within the skill of the routineer.

[0039] When the first and second anchor posts of an anchor pair are housed within the catheter prior to deployment, the distance between the first and second posts may be limited by the maximum diameter of the catheter. If both members of the anchor pair are affixed to the annulus simultaneously, then the initial distance between the first and second anchor posts is correspondingly limited. Increasing the effective diameter of the catheter, or at least of the portion of the catheter that accommodates the anchor posts, will allow simultaneous deployment of the first and second members of an anchor pair at a correspondingly greater initial distance from one another onto the annulus. To this end and others, the catheter may also include an expandable tip at its distal end that includes the housing for the first and second members of an anchor pair. For example, if the outer diameter of the catheter is 8 mm, the expandable tip may expand the distal end of the catheter that houses first and second anchor posts of an anchor pair to a final diameter of up to 20 mm. The expandable tip need not be fully expanded, such that the diameter of the at least partially expanded distal end of the catheter can be any diameter that exceeds the outer diameter of the catheter up to about 20 mm; for example, if the outer diameter of the catheter is 8 mm, the diameter of the at least partially expanded tip may be greater than 8 mm up to about 20 mm.

[0040] The catheter may further include one or more features for stabilizing the catheter while it is deployed at the annulus. Because the anchors should ideally be affixed to the center of a given section of annular tissue (*i.e.*, away from the margins of the annulus), and the physiological dimensions are small, precision maneuverability of the catheter is ideal. To this end and others, the distal end of the catheter may feature at least one lip. FIGS. 3A and 3B show a catheter 8 with a single lip 12 that, as shown in FIG. 3B, may rest on the interior margin of annulus 2. As catheter 8 is translated along the circumference of annulus 2 (for example, in the direction of arrow X), lip 12 functions as a guide that ensures the maintenance of contact between the catheter 8 and the inner margin of annulus 2. The catheter may also feature a further lip on the opposite side of the mouth (distal end) of the catheter, such that the further lip is

contacted with the outer margin of the annulus. Any further or alternative configurations may also be used for the catheter in order to enhance its stability at the annulus.

[0041] For illustrative purposes, FIG. 3B also depicts a pair of anchor posts 4c, 4d that have been affixed onto annulus 2 by having been propelled from catheter 8 into the tissue of annulus 2. Anchor posts 4c, 4d have been drawn together due to the vector force exerted by tensioner 6, thereby cinching the area S between posts 4c, 4d, as illustrated by wrinkling and bulging of the annulus at area S.

[0042] The kits may further comprise one or more of the following additional components: instructions for use; replacement parts for any of the components of the kits; and, tools for the repair of any component.

Example 1 – Reduction of Luminal Circumference, and Optionally of Septal-Lateral Axis

[0043] A kit is provided that includes a catheter according to the present invention with a single lip at the distal end; eight anchor pairs respectively consisting of a first and second anchor posts; and, silicone rubber tensioner rings. Additional components for performing the reduction procedure include: a 24 French Introducer sheath with dilator; cath lab access needles and catheters to gain access to the right femoral vein; transseptal equipment (including a Brockenbrough needle and Mullins sheath; and, sterile preparation for a cath lab procedure.

[0044] *Transseptal Access to the Left Atrium.* Access is obtained at the right femoral vein via a standard needle and guidewire for the placement of an 8 French Mullins sheath. The Mullins sheath is advanced over a guidewire into the superior vena cava, and then transseptal access to the left atrium is obtained with a Brockenbrough needle utilizing transesophageal echocardiographic guidance.

[0045] The patient is under general anesthesia with a transesophageal echocardiography (TEE) probe placed in the esophagus to guide both the transseptal procedure and the valve implantation as well. Once transseptal access to the left atrium is obtained, a standard extra-stiff guidewire is inserted into the left atrium through the Mullins sheath and utilized to exchange for the 24 French introducer sheath and dilator. This dilator is advanced into the left atrium, whereupon the guidewire and dilator is removed, and the sheath is flushed, thereby providing continuous access to the left atrium.

[0046] *Insertion and Positioning of the Catheter.* The catheter according to the present invention is loaded with a first anchor pair and tensioner, and inserted through the sheath into the left atrium. Once it exits from the delivery sheath, the catheter is steered with a combination of turning the sheath and turning the catheter to place the lip on the posterior lateral portion of the mitral annulus. Positioning is guided by both fluoroscopy and transesophageal

echocardiographic imaging. A stable and correct position is obtained and confirmed prior to delivery of either anchor post.

[0047] *Placement of Anchor Posts.* Anchor posts will then be deployed at an initial distance from each other of about 8 mm, which is also the diameter of the catheter. The members of the anchor pair are simultaneously propelled into the annulus, with the tensioner already extended between the members prior to deployment. Once both anchor posts are deployed the elastic tensioner pulls the respective posts towards each other, reducing the initial distance by about 30% to about 50% to provide a resulting distance and thereby cinching the corresponding portion of the posterior annulus over this short segment. Alternatively, a single member of the anchor pair is propelled into the annulus, and then, prior to propelling the second member of the anchor pair, the catheter is translated along the annulus up to about 1-2 cm, which results in greater spacing between the respective members of the anchor pair and therefore more absolute cinching of the corresponding portion of the annulus.

[0048] The catheter is then moved along the circumference of the annulus and the process repeated with further anchor pairs until a large portion of the total circumference is successfully cinched (shortened) by placement and tensioning of multiple anchor pairs. In some embodiments, a first anchor post of an anchor pair is affixed at the center of the posterior annulus and the second anchor post of the anchor pair is affixed at the center of the anterior annulus, with the tensioner stretched across the septal-lateral orifice of the valve, in order to provide septal-lateral cinching and reduction of the septal-lateral luminal dimension. This process may be repeated one or more times.

[0049] *Confirmation of Result.* Real time transesophageal echocardiography is used to assess the results in an ongoing fashion by examining the degree of mitral regurgitation and placement (cinching) of the annulus after each pair of anchor posts is deployed. The procedure is considered complete when an medically adequate degree of mitral regurgitation reduction has been achieved or there is no longer open space on the annulus on which to place anchor posts.

[0050] *Remove Catheter and Close Puncture.* The catheter is removed through the guiding sheath and the sheath is removed from the left atrium. The patient is heparinized for the procedure and once the heparin wears off the guide catheter is removed from the femoral vein and pressure manually applied to obtain hemostasis.

What is Claimed:

1. A method for reducing a luminal dimension of a mitral valve annulus of a subject comprising:
 - affixing a first anchor post onto a first location on said annulus;
 - affixing a second anchor post onto a second location on said annulus, said second location being an initial distance from said first location, and said first and second anchor posts collectively representing an anchor pair;
 - tensioning said first anchor post and said second anchor post using a tensioner that is stretched between said first and second anchor posts in order to give rise to a resulting distance between said first location and said second location, said resulting distance being less than said initial distance.
2. The method according to claim 1 wherein the degree of tensioning between said first and second anchor posts is chosen by selecting the coefficient of elastic recovery of the tensioner that is stretched between said first and second anchor posts.
3. The method according to claim 1 further comprising affixing first and second anchor posts of a further anchor pair onto respective locations on said annulus, and tensioning said first anchor post and said second anchor post of said further anchor pair.
4. The method according to claim 3 wherein the vector sum of said tensioning gives rise to a reduced luminal dimension.
5. The method according to claim 4 comprising reducing the luminal circumference.
6. The method according to claim 5 wherein the luminal circumference is reduced up to about 30%.
7. The method according to claim 1 further comprising affixing first and second anchor posts of a plurality of further anchor pairs on said annulus, and tensioning said first anchor post and said second anchor post of each respective further anchor pair.
8. The method according to claim 1 wherein said first location on said annulus is adjacent to said second location on said annulus.

9. The method according to claim 1 wherein said first location is about 5 to about 15 mm from said second location.
10. The method according to claim 1 wherein said first location is substantially across the short axis of said annulus from said second location.
11. The method according to claim 1 wherein said resulting distance is about 5% to about 60% less than said initial distance.
12. The method according to claim 1 wherein said first anchor post is affixed onto said first location and said second anchor post is affixed onto said second location by propelling said first and second anchor posts into said annulus.
13. The method according to claim 12 wherein said first and second anchor posts are propelled from a catheter into said annulus.
14. The method according to claim 1 wherein said tensioner is extended between said first and second anchor posts prior to affixing said first and second anchor posts onto said annulus.
15. The method according to claim 1 wherein said first and second anchor posts are affixed onto the atrial side of said annulus.
16. The method according to claim 1 wherein said first and second anchor posts are affixed onto the ventricular side of said annulus.
17. A kit for use in reducing a luminal dimension of a mitral valve annulus of a subject comprising:
 - a steerable catheter comprising a proximal end and a distal end, the proximal end being operably associated with a steering mechanism;
 - a plurality of anchor pairs respectively comprising first and second anchor posts, said distal end of said catheter being configured for housing an anchor pair and for affixing an anchor pair onto said annulus; and,
 - a material for tensioning the first and second anchor posts of each respective anchor pair when said first and second anchor posts are affixed onto said annulus.

18. The kit according to claim 17 comprising at least about five anchor pairs and material for tensioning the posts of each of said anchor pairs.
19. The kit according to claim 17 wherein said catheter is configured for affixing an anchor pair onto said annulus by propelling said first and second anchor posts into said annulus.
20. The kit according to claim 17 wherein said distal end of said catheter comprises a lip for stabilizing said catheter while deployed at said annulus.
21. The kit according to claim 17 wherein said material is an elastic material

1/1
FIG. 1

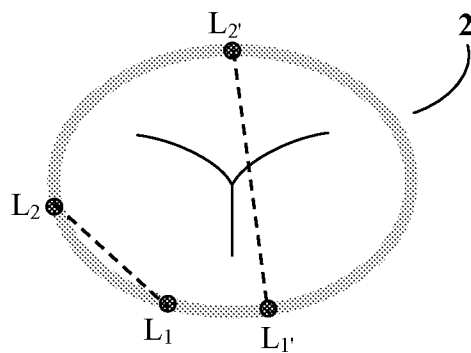


FIG. 2

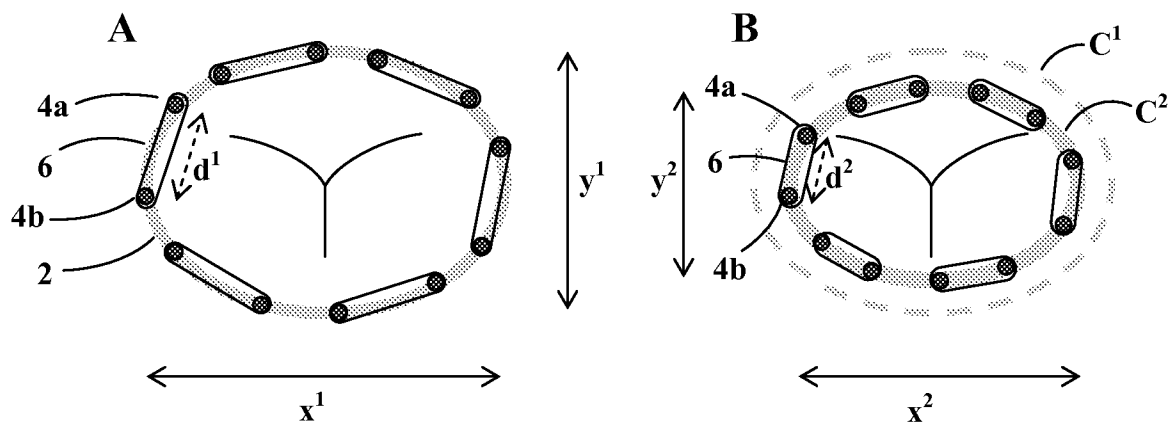
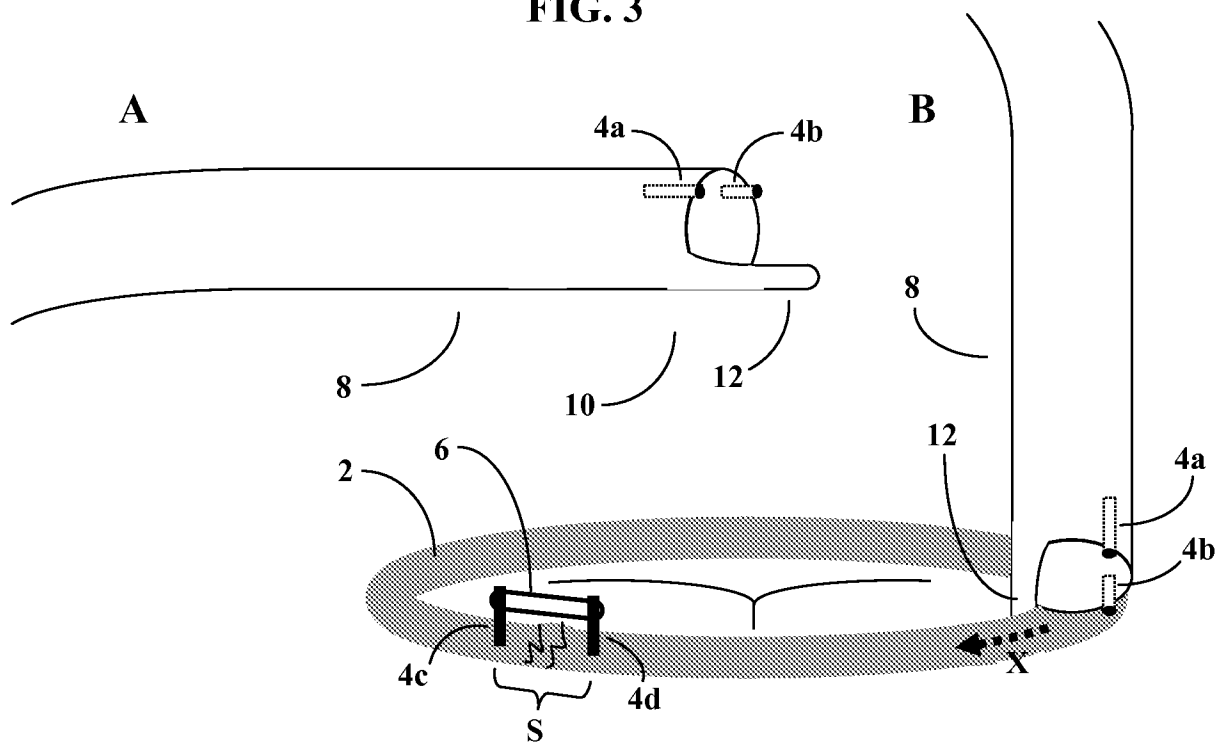


FIG. 3



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US13/35222

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 17/08 (2013.01)

USPC - 606/151, 219, 153

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): A61B 17/08 (2013.01)

USPC: 606/151, 219, 153

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); IP.com; DialogPRO; PubMed/Medline; Google/Google Scholar: reduc*3, decreas*3, minimiz*3, shorten*3, "mitral valve annulus", dimension*1, size*1, first, second, anchor*1, post*1, pin*1, rod*1, attachment*1, location*1, position*1, tension*3, tighten*3, pull*3, shorten*3, initial, predetermined, distance

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2005/0065550 A1 (STARKSEN, NF et al.) March 24, 2005; figure 10F; paragraphs [0047], [0049], [0063], [0065], [0070]-[0075]	1, 3, 7-8, 12-21 ----- 2, 4-6, 9-11
X --- Y	US 6913608 B2 (LIDDICOAT, JR et al.) July 5, 2005; figures 3, 4, 7, 33; column 7, lines 4-16; column 6, lines 29-41, 55-64; column 11, lines 62-67	1 ----- 4-6, 9-11
Y	US 2010/0023056 A1 (JOHANSSON, PK et al.) January 28, 2010; figures 1B, 10F; paragraphs [0041], [0111]	2

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

11 June 2013 (11.06.2013)

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