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Canadian Intellectual Property Office

CA 3012709 C 2022/07/12

(11)(21) 3 012 709

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 2017/03/10
(87) Date publication PCT/PCT Publication Date: 2017/09/21
(45) Date de délivrance/Issue Date: 2022/07/12
(85) Entrée phase nationale/National Entry: 2018/07/25
(86) N° demande PCT/PCT Application No.: US 2017/021719
(87) N° publication PCT/PCT Publication No.: 2017/160610
(30) Priorités/Priorities: 2016/03/18 (US62/310,044); 2016/06/06 (US62/346,214); 2016/08/23 (US62/378,258); 2016/12/20 (US62/436,750)

(51) Cl.Int./Int.Cl. *A61N 1/375* (2006.01), *A61B 5/287* (2021.01), *A61M 25/09* (2006.01), *A61N 1/05* (2006.01)

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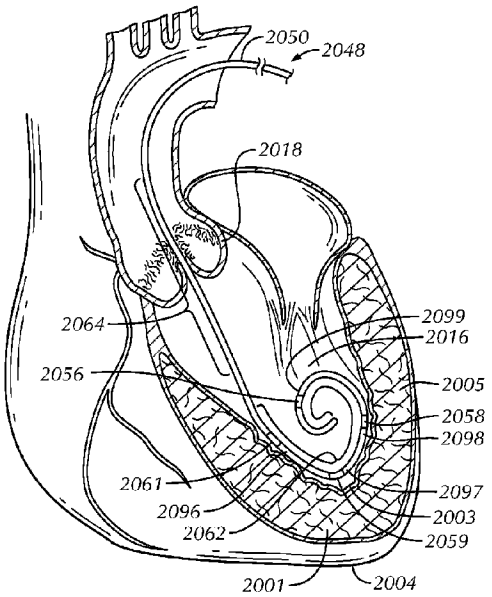
(54) Titre : FIL-GUIDE DE STIMULATION
(54) Title: PACING GUIDEWIRE




(57) Abrégé/Abstract:
Guidewires and methods for transmitting electrical stimuli to a heart and for guiding and supporting the delivery of elongate treatment devices within the heart are disclosed. A guidewire can comprise an elongate body, including first and second elongate conductors, and at least first and second electrodes. A distal end portion of the elongate body can include a preformed bias shape, such as a pigtail- shaped region, on which the first and second electrodes can be located. The preformed bias shape can optionally be non-coplanar relative to an intermediate portion of the elongate body. The first and second elongate conductors can be formed of a single structure or two or more electrically connected structures. The conductors can extend from proximal end portions to distal end portions that electrically connect to the first and second electrodes. A corewire can extend the length of the elongate body, can at least partially form the first conductor, and can be at least partially surrounded by the second conductor.

CA 3012709 C 2022/07/12
(11)(21) 3 012 709
(13) C

(73) Propriétaires(suite)/Owners(continued):CARDIAC INTERVENTIONS AND AVIATION LLC, US
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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 September 2017 (21.09.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/160610 A1

(51) International Patent Classification:
*A61N 1/375* (2006.01) *A61B 5/042* (2006.01)
*A61B 5/00* (2006.01) *A61N 1/05* (2006.01)

(21) International Application Number:
PCT/US2017/021719

(22) International Filing Date:
10 March 2017 (10.03.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

| | | |
|---|---|---|
| 62/310,044 | 18 March 2016 (18.03.2016) | US |
| 62/346,214 | 6 June 2016 (06.06.2016) | US |
| 62/378,258 | 23 August 2016 (23.08.2016) | US |
| 62/436,750 | 20 December 2016 (20.12.2016) | US |


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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

*[Continued on next page]*

(54) Title: PACING GUIDEWIRE

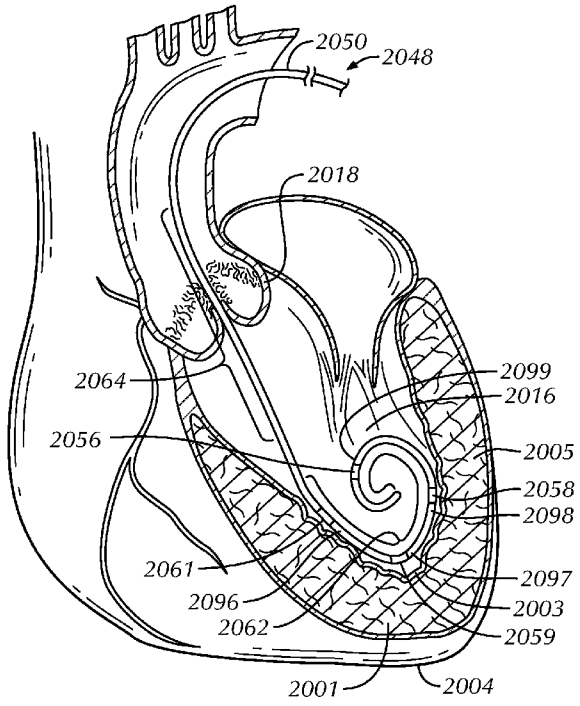


*FIG. 20*

(57) Abstract: Guidewires and methods for transmitting electrical stimuli to a heart and for guiding and supporting the delivery of elongate treatment devices within the heart are disclosed. A guidewire can comprise an elongate body, including first and second elongate conductors, and at least first and second electrodes. A distal end portion of the elongate body can include a preformed bias shape, such as a pigtail- shaped region, on which the first and second electrodes can be located. The preformed bias shape can optionally be non-coplanar relative to an intermediate portion of the elongate body. The first and second elongate conductors can be formed of a single structure or two or more electrically connected structures. The conductors can extend from proximal end portions to distal end portions that electrically connect to the first and second electrodes. A corewire can extend the length of the elongate body, can at least partially form the first conductor, and can be at least partially surrounded by the second conductor.

WO 2017/160610 A1

WO 2017/160610 A1

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

**(84) Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published**:

— *with international search report (Art. 21(3))*

# PACING GUIDEWIRE

## CLAIM OF PRIORITY

Benefit of priority is hereby claimed to Daniels et al., U.S. Provisional Patent Application Serial Number 62/310,044, entitled "PACING GUIDEWIRE" and filed on March 18, 2016, to Daniels et al., U.S. Provisional Patent Application Serial Number 62/346,214, entitled "PACING GUIDEWIRE" and filed on June 6, 2016, to Daniels et al., U.S. Provisional Patent Application Serial Number 62/378,258, entitled "PACING GUIDEWIRE" and filed on August 23, 2016, and to Daniels et al., U.S. Provisional Patent Application Serial Number 62/436,750, entitled "PACING GUIDEWIRE" and filed on December 20, 2016.

## TECHNICAL FIELD

This patent document relates to medical devices. More particularly, but not by way of limitation, the patent document relates to guidewires.

## BACKGROUND

Heart valve replacement may be indicated when there is a narrowing of a native heart valve or when the native valve leaks or regurgitates, such as when the valve's leaflets are calcified.

The native valve can be excised and replaced with either a biologic tissue valve or a mechanical valve. Mechanical valves require lifelong anticoagulant medication to prevent blood clot formation, and clicking of the valve can often be heard through a patient's chest. Biologic tissue valves typically do not require such medication and do not click. Tissue valves can be obtained from cadavers or can be porcine or bovine based, and the valves can be attached to cloth-covered synthetic rings or leaflet support frames that are securable to a patient's heart valve annulus.

Conventional heart valve surgery is an open heart procedure conducted under general anesthesia with significant concomitant risks, including bleeding, infection, stroke, heart attack, arrhythmia, renal failure, adverse reactions to the anesthesia medications, or sudden death. An incision is made through the patient's sternum, and the patient's heart is stopped while blood flow is rerouted through a heart-lung bypass machine. The first two or three days following conventional heart valve surgery are often spent in an intensive care unit where heart functions can be closely monitored. The average hospital stay following conventional heart valve surgery is between one and two weeks, with several more weeks required for complete recovery.

Advancements in minimally-invasive surgery and interventional cardiology have encouraged some physicians to pursue percutaneous replacement of a heart valve, including the deployment of an expandable prosthetic heart valve device across the native diseased heart valve (which permanently holds the native valve open). The prosthetic heart valve device can be designed for percutaneous delivery in a cardiac catheterization laboratory under local anesthesia using fluoroscopic guidance, thereby avoiding general anesthesia and open-heart surgery.

## OVERVIEW

The present inventors recognize that guidewires play an important role in the field of percutaneous replacement of a heart valve, including percutaneous transcatheter aortic valve implantation (TAVI), transcatheter aortic valve replacement (TAVR), balloon valvuloplasty (BV) or transcatheter mitral valve replacement (TMVR). The present inventors further recognize that there is a need for guidewires and related methods that can reduce the time for, and increase the chances of, a successful percutaneous implantation of a prosthetic heart valve device.

This patent document discloses pacing guidewires that facilitate the performance of TAVI, TAVR, BV or TMVR procedures by (i) providing good

support for the over-the-wire (OTW) delivery of elongate treatment devices with low chance of perforation or other damage of vessels, the native aortic or mitral valve, or cardiac tissues through which the guidewire is inserted, and (ii) inducing and maintaining cardiac ventricular tachycardia during certain phases of such procedures. A pacing guidewire can comprise an elongate body, including first and second conductors, and at least first and second electrodes. The elongate body can extend from a proximal end portion to a distal end portion with an intermediate portion therebetween. The at least first and second electrodes have one of a positive or negative polarity and can be spaced between 1 centimeter (cm) and 10cm apart, for example, in varying configurations along a preformed bias shape at the distal end portion of the elongate body. The first elongate conductor can extend from a proximal end portion to a distal end portion that is electrically connected to the first electrode. Similarly, the second elongate conductor can extend from a proximal end portion to a distal end portion that is electrically connected to the second electrode.

A method for transmitting electrical stimuli to a patient's heart and for guiding and supporting the OTW delivery of elongate treatment devices within the heart can include advancing a distal end portion of a pacing guidewire into a patient's left ventricle such that first and second electrodes are positioned against or near a ventricular wall. Electrical stimuli can be transmitted through the guidewire to the first and second electrodes to induce and maintain cardiac ventricular tachycardia. In various examples, the electrical stimuli transmitted through the guidewire can result in a current flow of 4.0mA or less, 3.0mA or less, 2.5mA or less, or 2.0mA or less between the electrodes. While the heart is in a state of ventricular tachycardia, a medical procedure, such as dilatation balloon expansion within a native aortic or mitral valve, can be performed.

In accordance with an aspect of the present invention, is a pacing guidewire, comprising:

an elongate body having an outer diameter ranging from about 0.36mm (0.014in) to about 0.97mm (0.038in) and configured to receive and to support delivery of an elongate treatment device that is advanced over the pacing guidewire, the elongate body extending from a proximal end portion of the pacing guidewire to

a distal end portion of the pacing guidewire and having an intermediate portion therebetween, the distal end portion including a preformed bias shape; and

at least first and second electrodes spaced apart on the preformed bias shape, one of the electrodes serving as an anode and the other electrode serving as a cathode for delivering pacing pulses to a heart of a patient while the elongate body supports delivery of the elongate treatment device to the heart of the patient,

the elongate body including a first elongate conductor, which extends from the proximal end portion to the distal end portion that is electrically connected to the first electrode, and a second elongate conductor, which is insulated from the first elongate conductor and extends from the proximal end portion to the distal end portion that is electrically connected to the second electrode.

In accordance with a further aspect is a left ventricular pacing guidewire, comprising:

an elongate body having an outer diameter ranging from about 0.36mm (0.014in) to about 0.97mm (0.038in), and configured to receive and to support delivery of an elongate treatment device that is advanced over the pacing guidewire, the elongate body extending from a proximal end portion of the pacing guidewire to a distal end portion of the pacing guidewire and having an intermediate portion therebetween, the distal end portion including a first region configured to contact a first ventricular wall of a heart on a first side of a ventricular apex, a second region configured to span across the ventricular apex, a third region configured to contact a second ventricular wall on a second side of the ventricular apex, and a fourth region configured to curve away from the second ventricular wall on the second side of the ventricular apex;

a first electrode disposed on the fourth region and spaced from the first and second ventricular walls; and

a second electrode, a third electrode and a fourth electrode disposed on one of the first region, the second region or the third region,

the elongate body including a first elongate conductor, which extends from a proximal end portion to a distal end portion that is electrically connected to the first electrode, and a second elongate conductor, which is insulated from the first

elongate conductor and extends from a proximal end portion to a distal end portion that is electrically connected to the second, third and fourth electrodes.

In accordance with a further aspect is a left ventricular guidewire, comprising:

means for concurrently supporting delivery of an aortic valve treatment device and for inducing and maintaining cardiac ventricular tachycardia,

wherein the means includes insulated anode and cathode poles positioned on a distal pigtail-shaped region such that a first pole is positionable away from a ventricular wall of a heart during pacing and a second pole is positionable in contact with the ventricular wall during pacing,

and wherein the pigtail-shaped region transmits applied insertion forces along a dispersed, radial path.

In accordance with a further aspect, is the use of a bipolar pacing guidewire for performing a medical procedure on a heart:

wherein a distal end portion of the bipolar pacing guidewire is for advancing into a left ventricle of a patient's heart, and for positioning first and second electrodes against or spaced from a left ventricular wall; and

wherein electrical stimuli are for transmitting through the guidewire to the first and second electrodes for inducing and maintaining cardiac ventricular tachycardia for performing said medical procedure.

These and other examples and features of the present pacing guidewires and methods will be set forth, at least in part, in the following Detailed Description. This Overview is intended to provide non-limiting examples of the present teachings—it is not intended to provide an exclusive or exhaustive explanation. The Detailed



Date Reçue/Date Received 2020-05-14

Description below is included to provide further information about the present guidewires and methods.

## BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, like numerals can be used to describe similar features and components throughout the several views. The drawings illustrate generally, by way of example, but not by way of limitation, various embodiments discussed in this patent document.

FIG. **1** is a schematic illustration of the implantation of a prosthetic aortic heart valve using a conventional guidewire and a dedicated right ventricular lead pacing means.

FIG. **2** is a schematic illustration of an example pacing guidewire configured to transmit electrical stimuli from an external pulse generator to the heart and guide and support the OTW delivery of elongate treatment devices.

FIG. **3** is an enlarged schematic illustration of a proximal end portion of an example pacing guidewire.

FIG. **4** is a schematic illustration of an example connector body, which is removably couplable to a proximal end portion of a pacing guidewire.

FIGS. **5-8** are enlarged schematic illustrations, in longitudinal cross-section, of intermediate portions of example pacing guidewires.

FIGS. **9-14** are enlarged schematic illustrations of distal end portions of example pacing guidewires.

FIG. **15** is a schematic illustration of an example electrical connection between two structures forming an elongate conductor, such as the electrical connection at portion labeled **15** of the pacing guidewire of FIG. **10**.

FIG. **16** is a schematic illustration of an example insulation configuration to electrically isolate first and second elongate conductors, such as the insulation configuration at portion labeled **16** of the pacing guidewire of FIG. **10**.

FIGS. **17-19** are enlarged schematic illustrations of example electrode configurations designed to stimulate heart tissue.

FIG. **20** is a schematic illustration of an example pacing guidewire positioned within a left ventricle of a heart.

FIG. **21** is a graph illustrating invasive blood pressure (top), an intracardiac electrocardiogram (middle), and pacing spikes (bottom) during rapid left ventricular pacing of a pig's heart using an example pacing guidewire.

FIG. **22** is a diagnostic image illustrating an example pacing guidewire supporting the delivery of a heart valve system.

FIG. **23** is a schematic illustration of the implantation of a prosthetic aortic heart valve using an example pacing guidewire and an external pulse generator.

The drawing figures are not necessarily to scale. Certain features and components may be shown exaggerated in scale or in schematic form, and some details may not be shown in the interest of clarity and conciseness.

## DETAILED DESCRIPTION

Definitions:

Certain terms are used throughout this patent document to refer to particular features or components. As one skilled in the art will appreciate, different people may refer to the same feature or component by different names. This patent document does not intend to distinguish between components or features that differ in name but not in function. For the following defined terms, certain definitions

shall be applied unless a different definition is given elsewhere in this patent document.

The terms "proximal" and "distal" refer to a position or direction relative to a treating physician. "Proximal" and "proximally" refer to a position that is closer to, or in a direction toward, the physician. "Distal" and "distally" refer to a position that is distant, or in a direction away, from the physician and opposite the proximal direction.

The term "patient" refers to mammals and includes both humans and animals.

The singular forms "a", "an", and "the" include plural referents unless the content clearly dictates otherwise. As used in this specification and the appended claims, the term "or" is generally employed in its sense including "and/or" unless the content clearly dictates otherwise.

All numeric values are assumed to be modified by the term "about," whether or not explicitly indicated. The term "about" refers to a range of numbers that one of skill in the art would consider equivalent to the recited value (e.g., having the same function or result). In many instances, the term "about" can include numbers that are rounded to the nearest significant figure.

The recitation of numerical ranges by endpoints includes all numbers and sub-ranges within and bounding that range (e.g., 1 to 4 includes 1, 1.5, 1.75, 2, 2.3, 2.6, 2.9, etc. and 1 to 1.5, 1 to 2, 1 to 3, 2 to 3.5, 2 to 4, 3 to 4, etc.).

Existing transfemoral TAVI, TAVR, BV and TMVR procedures:

FIG. **1** is a schematic illustration of a prosthetic aortic heart valve **102** being implanted into a heart **104** using a conventional guidewire **106**. The heart **104** includes a right atrium **110**, a left atrium **112**, a right ventricle **114** and a left ventricle **116**. The left ventricle **116** connects to a body's arteries by way of an aortic valve **118** and an ascending aorta **120**. As part of the valve implantation procedure, the guidewire **106** can be inserted through a guide catheter that extends

from a femoral artery **122**, through the ascending aorta **120**, and within the aortic valve **118** of the patient. The guidewire **106** can be advanced through the guide catheter until its distal end portion locates, or nests against, the apex **124** of the left ventricle **116**. With the guidewire **106** positioned inside the heart **104** and serving as an OTW support structure for the rest of the valve implantation procedure, the guide catheter can be removed from the patient.

An introducer sheath **126** can be inserted over the guidewire **106** and into the ascending aorta **120**, and subsequently a balloon catheter **128** having a dilatation balloon **130** on its distal end portion can be passed over the guidewire and through the sheath. A physician can locate a distal tip **132** of the introducer sheath **126** using a radiopaque marker(s) **134** and fluoroscopy, or using other imaging systems such as transesophageal echo, transthoracic echo, intravascular ultrasound imaging (IVUS), or an injectable dye that is radiopaque. The dilatation balloon **130** can be expanded radially outward into contact with native aortic valve leaflets **136** as part of a BV procedure. With information concerning the size of the particular aortic valve **118**, the balloon **130** can be chosen so that it expands outward and nominally compresses the aortic valve leaflets **136** against surrounding aortic walls **138**.

The physician or operating room staff can then crimp the expandable prosthetic aortic heart valve **102** over the dilatation balloon **130**. Currently, there are two primary expandable prosthetic heart valves **102** available in the U.S. to select from—the Edwards-Sapien™ heart valve (Edwards Lifesciences, Irvine, CA) and the CoreValve™ device (Medtronic, Minneapolis, MN). The Edwards-Sapien is a tri-leaflet bovine pericardial valve within a tubular balloon expandable stent. Both retrograde (i.e., transfemoral) and antegrade (i.e., transapical) approaches can be used depending on patient characteristics. The CoreValve is a tri-leaflet porcine pericardial valve with a self-expanding nitinol stent. This valve can be used via a retrograde approach via transfemoral, subclavian, axillary or direct aortic access.

With the prosthetic heart valve **102** crimped over the balloon **130**, the physician can once again advance the balloon catheter **128** over the guidewire **106**

and through the introducer sheath **126** until the prosthetic heart valve is located at the aortic annulus between the native aortic leaflets **136**. When the physician is satisfied with the positioning and rotational orientation of the prosthetic heart valve **102**, the balloon **130** can be expanded into gripping contact with the aortic annulus. The term "gripping contact" can imply sufficient contact to ensure that the prosthetic heart valve **102** does not migrate after expansion. Once the valve **102** is properly implanted, the physician can deflate the balloon **130** and withdraw the balloon catheter **128** over the guidewire **106**. The introducer sheath **126** can then be withdrawn simultaneously with, or followed by, the guidewire **106**.

During existing TAVI, TAVR, BV and TMVR procedures, temporary right ventricular rapid pacing **108**, which has been associated with a small but recognized rate of morbidity, is performed in order to induce and maintain a ventricular tachycardia. The ventricular tachycardia can lower the patient's blood pressure to allow balloon deployment in the aortic annulus without balloon embolization from cardiac flow, and it can assure more accurate placement of the prosthetic heart valve **102** being implanted. The traditional way of temporary pacing involves a femoral or jugular venous puncture to place the distal end portion of a unipolar pacing lead **140** in or on a wall of the right ventricle **114**. A proximal end portion of the lead **140** can be connected to a first pole of an external pulse generator **142** with an alligator clamp, and a second opposite pole of the external pulse generator **142** can be electrically connected to a large surface skin electrode **144** placed at a left thigh **146** of the patient, for example. The skin electrode **144** can be used as a return electrode for the single lead electrode.

In an effort to streamline TAVR and other valve-related procedures and avoid attendant complications, the present inventors have investigated use of a 0.035in (0.89mm) left ventricular delivery wire as a pacing lead. Though this concept is conceptually appealing, in practice the use of guidewires for pacing is challenging since existing wires are not insulated against current loss in blood and therefore: cannot be tested for ventricular capture until they are insulated within a

patient's body such as with a valvuloplasty balloon or a TAVR device; cannot provide obligate pacing following TAVR without the valvuloplasty balloon or TAVR device left in place; can only provide unipolar pacing in conjunction with a grounding contact in or on subcutaneous tissue and a non-dedicated connection to an electrical source; and have high pacing capture thresholds and low safety margins due to unipolar pacing.

The guidewires and methods disclosed in this patent document include a purpose built rail device with insulated poles capable of consistent left ventricular pacing at low thresholds with or without a delivery system (e.g., a valvuloplasty balloon or a TAVR device) in place. The pacing guidewires and related methods can improve procedural safety and efficiency by providing the dual purpose of (i) transmitting electrical stimuli to the heart **104** for inducing and maintaining a ventricular tachycardia, and (ii) guiding and supporting the OTW delivery of elongate treatment devices (e.g., a balloon catheter) for successful implantation of the prosthetic aortic heart valve **102**. It is believed that pacing the heart **104** using a left ventricular bipolar guidewire can be a beneficial alternative to conventional transvenous temporary right ventricular pacing **108** in the context of TAVI, TAVR, BV and TMVR procedures. Among other things, this pacing alternative obviates the need for an additional venous puncture and avoids the cost, discomfort, and risk of perforating the right ventricle **114** with the temporary unipolar pacing lead **140**.

In the description that follows, the present pacing guidewires are shown as having a design that is optimized for use in connection with TAVI, TAVR or BV procedures. For example, a guidewire can be designed with a sufficient degree of flexibility to facilitate negotiation of tortuous anatomy and to minimize trauma to cardiac tissue, while also maintaining a certain level of stiffness, particularly in the aortic valve region, in order to provide adequate support for items delivered thereon (e.g., aortic valve implantation systems) and to sit comfortably within the left ventricle **116** in a stable, atraumatic manner. It should be noted, however, that the present pacing guidewires are not limited to use in TAVI, TAVR and BV

procedures. The guidewires could be similarly utilized in a wide variety of percutaneous medical procedures, such as gastrointestinal or hepatobiliary procedures, as well as alternative types of coronary procedures such as TMVR, without departing from the scope of the present patent document.

Pacing guidewires of present subject matter:

FIG. **2** is a schematic illustration of a pacing guidewire **248** including an elongate body **250** carrying a first elongate conductor **252**, a second elongate conductor **254**, and at least two electrodes **256**, **258** for delivering electrical stimuli to a heart, such as to a left ventricle of the heart. Portions of the elongate body **250** can include a lubricious coating (e.g., a coating including hydrophilic, polytetrafluoroethylene (PTFE), silicone or other dry lubricious material) to ease its advancement through a guide catheter and to facilitate the OTW delivery and withdrawal of devices guided over it. In an example, a first portion of the elongate body **250** has a silicone coating and a second portion of the body has a hydrophilic coating. The coating(s) can be applied by dip coating, spraying, or shrink wrapping a hollow tube of such material over the outer surface of the elongate body **250**.

Indicia suitable for viewing by a physician, thereby providing a distinguishing characteristic from non-pacing guidewires and other interventional tools that may be used during a procedure, can be applied to the coating(s) or the elongate conductors **252**, **254**. The indicia can be applied to the coating(s) before or after their application to the elongate body **250**. Alternatively, the indicia can be applied to the conductors **252**, **254** and a transparent coating can be applied over the conductors for visibility of the indicia. The indicia can include one or more continuous helical strips, individual discontinuous circumferential stripes, or other axially spaced apart indicia along the length of the guidewire. The indicia can be bi-color, tri-color, or any combination of colors that are discernable. The indicia can be about 1mm to 4mm wide and spaced apart by a similar distance for clarity. The

indicia can extend over the entire length of the elongate body **250** or solely over a certain portion(s) of the length.

The elongate body **250** can extend from a proximal end portion **260** to a distal end portion **262**, with an intermediate portion **264** therebetween. The proximal end portion **260** can be manipulated by the physician from a position outside of a patient's body. The distal end portion **262** can include a flexible tip to facilitate traversal through the body to one or more target pacing sites. The elongate body **250** can have any suitable length for use in conducting electrical stimuli from an external pulse generator **242** to the heart of the patient, such as from about 100cm to about 300cm. The elongate body **250** can have a circular cross-section for facilitated insertion through portions of the body. The diameter of the elongate body **250**, including insulation, can be in the range of about 0.014in (0.36mm) to about 0.038in (0.97mm), such as about 0.035in (0.89mm), although other sizes are also possible.

The first and second conductors **252**, **254** allow the guidewire **248** to function as a bipolar pacing wire. The first conductor **252** can extend longitudinally from a terminal contact at a proximal end portion **266**, through or along the elongate body **250**, to a distal end portion **268** electrically connected to at least the first electrode **256**. The second conductor **254** can similarly extend longitudinally from a terminal contact at a proximal end portion **270**, through or along the elongate body **250**, to a distal end portion **272** electrically connected to at least the second electrode **258**. Each conductor **252**, **254** can be formed of a single structure or multiple structures, which are electrically joined together such as by soldering or welding. The conductors **252**, **254** can be highly flexible small diameter metal filaments, stranded cables, helical coils constructed of circular wire or flat wire (allowing for diametrical space savings), corewires, braids, hypotubes or electrically-conductive polymer layers constructed from a conductive, low resistance material, such as MP35N® alloy (SPS Technologies, Jenkintown, PA), Elgiloy® alloy (Elgiloy Specialty Metals, Sycamore, IL), tungsten, platinum, silver, stainless steel, polyacetylene or combinations thereof, for example.

The first and second electrodes **256**, **258** can be coaxially or eccentrically mounted along the elongate body **250** and can spaced apart by a predetermined distance, such as a distance between about 1cm and 10cm, with insulation in between. In some examples, more than two electrodes—such as three, four or five electrodes—can be mounted along the elongate body **250**. The electrodes **256**, **258** can be cylindrical in shape and can have an axial length between about 2mm and about 20mm, for example, for delivery of electrical stimuli to the heart. At least one electrode can serve as the anode and at least one other electrode can serve as the cathode. The present inventors have found that limiting the collective axial length of cylindrical electrodes of each polarity to 12mm or less, and particularly 10mm or less, can provide a beneficial, more concentrated current density to heart tissue. For example, if the second conductor **254** is electrically connected to three cylindrical electrodes, the collective axial length of those three electrodes can be 12mm or less, or 10mm or less. Alternatively, one of both of the electrodes **256**, **258** can have a non-cylindrical, strip-like (channel-like) shape axially extending for lengths between about 1cm and 10cm, for example. Each electrode can be made up of one strip or multiple strips. The strip(s) can be straight and extend along one side of the guidewire or can have a spiral configuration that wraps around the guidewire.

In operation, AC stimuli signals created by the external pulse generator **242** can be applied to the electrodes **256**, **258**. The pulse generator **242** can include means for delivering time-spaced pulses to the electrodes **256**, **258** for suitable pacing. Current on the order of about 4.0mA or less, 3.0mA or less, 2.5mA or less, or 2.0mA or less, for example, can flow through blood or other fluid between the spaced apart electrodes **256**, **258**.

FIG. **3** is an enlarged schematic illustration of a proximal end portion **360** of an example pacing guidewire's elongate body **350**. In this example, a first conductor **352** can be at least partially in the form of a corewire, and a second conductor **354** can be at least partially in the form of a braid or hypotube. Each conductor **352**, **354** can include a dedicated terminal contact brought out from the elongate body **350** at

its proximal end portion **366**, **370**. The terminal contacts can be in-line with one another for direct electrical connection with an external pulse generator **342** via a generator receptacle **371**, or indirect electrical connection with the pulse generator **342** via a dedicated connector body. Any other suitable method of effecting electrical connection between the conductors **352**, **354** and the pulse generator **342** can also be employed.

FIG. **4** is a schematic illustration of an example connector body **474** removably couplable to a proximal end portion of a pacing guidewire's elongate body. The connector body **474** can include a guidewire connection portion **475** and pulse generator connection portions **477*a***, **477*b***. The guidewire connection portion **475** can be slid on and off the proximal end portion of the pacing guidewire's elongate body and can include an entrance seal member to electrically isolate conductors of the pacing guidewire from bodily and medical fluids present in the treatment area. The pulse generator connection portions **477*a***, **477*b*** can provide an electrical extension of the guidewire's conductors and can be color-coded or otherwise marked for identification of each conductor's polarity. In this example, pulse generator connection portion **477*a*** has a negative polarity (cathode) and pulse generator connection portion **477*b*** has a positive polarity (anode). The pulse generator connection portions **477*a***, **477*b*** can make electrical connections with the pulse generator by way of alligator clips, for example.

FIGS. **5-8** are enlarged schematic illustrations, in section, of intermediate portions **564**, **664**, **764**, **864** of an example pacing guidewire's elongate body **550**, **650**, **750**, **850**. The elongate body **550**, **650**, **750**, **850** can include one or more tapers and constant diameter regions, which can be manifested in variations in the size of the outer diameter, the inner diameter and the wall thickness of body components. Any tapers and constant diameter regions can be formed by any one of a number of different techniques, for example, by centerless grinding methods, stamping methods, extrusion methods, co-extrusion methods, and the like.

A corewire **580**, **680**, **780**, **880** can extend from a proximal end portion to a distal end portion of the elongate body **550**, **650**, **750**, **850**. The corewire can have a gradual reduction (or taper) **582**, **682**, **882** in its cross-sectional diameter through the intermediate portion **564**, **664**, **864**, as shown in the examples of FIGS. **5**, **6** and **8**. This gradual reduction **582**, **682**, **882** can provide the elongate body **550**, **650**, **850** with a diminishing degree of stiffness and increased flexibility towards its distal end portion. By enhancing its flexibility, the distal end portion of the elongate body **550**, **650**, **850**, which can be designated for placement against sensitive myocardial tissues and structures, is less likely to impart potentially harmful forces. At the same time, the intermediate portion **564**, **664**, **764**, **864** can maintain an adequate degree of stiffness to support the OTW delivery of critical components, such as a dilatation balloon or a prosthetic aortic valve.

The transition in cross-sectional diameter along the corewire **580**, **680**, **880** can be provided in a subtle manner to render the guidewire more resistant to kinking upon the application of stress. The present inventors have found that regions in a corewire with rapid transitions in cross-sectional diameter are more susceptible to the formation of sharpened bends or kinks during use. The creation of sharpened bends or kinks in the corewire can be problematic in that they can introduce traumatic forces against a point on a ventricular wall, for example, thereby perforating or otherwise damaging heart tissue, and can catch on a device slidably mounted over the guidewire.

As shown in the examples of FIGS. **5-7**, the corewire **580**, **680**, **780** can be made from an electrically-conductive material and, as such, can at least partially form one of the guidewire's conductors **552**, **652**, **752**, while the second of the guidewire's conductors **554**, **654**, **754** can surround a portion of the corewire and can take the form of a helical coil **584** (FIG. **5**), an electrically-conductive polymer layer **686** (FIG. **6**), a hypotube **788** (FIG. **7**), a braid or a combination thereof.

In the example of FIG. **5**, the helical coil **584** can be secured to the corewire **580** at each of its ends using a bonding agent, such as an electrically-insulating, non-

conductive epoxy, but otherwise free-floating relative to the corewire **580**. The helical coil **584** can be a single filar coil or a multi-filar coil.

In the example of FIG. **6**, the electrically-conductive polymer **686** can be of tubular form or alternatively in the form of a tape that is helically wrapped about the corewire **680**. Conductive polymers fall into two general categories: intrinsically conductive and conductor-filled. Intrinsically conductive polymers can include polyacetylene, polypyrrole and polyaniline, among others. Alternatively, conductor-filled polymers can include presently available materials approved for implantation such as silicone rubber with embedded metallic, carbon or graphite particles or powder.

In the example of FIG. **7**, the corewire **780** can be concentric and slide inside the hypotube **788**. This design can enable a proximal electrode to be placed at a desired location, and a distal electrode can be extended a variable distance beyond the proximal electrode.

As shown in the example of FIG. **8**, the corewire **880** can be electrically neutral and at least partially surrounded by first and second conductors **852**, **854** in the form of helical coils **884*a***, **884*b***. Two conductive wires can be in coaxially wound into a single helical form. The wires can be insulated from one another prior to winding and can optionally be of differing diameters, as shown in the example of FIG. **17**. Alternatively, a first conductor can be wound into a helical coil of a diameter less than a winding of a second conductor.

The helical coil(s) **584**, **884*a***, **884*b***, electrically-conductive polymer layer **686**, or hypotube **788** can extend a substantial length of the corewire **580**, **680**, **780**, **880** or can extend solely around its proximal end, intermediate **564**, **664**, **764**, **864**, and/or distal end portions. The present inventors have found that helical coils extending the entire length of the corewire require electricity to travel a relatively long distance and can increase the electrical resistance associated with an electrical path between an external pulse generator and distally-positioned electrodes. Accordingly, a low resistance linear filament, stranded cable, hypotube, or braid can

be used to travel a portion of the length of the corewire and bridge the electrical path between the external pulse generator and an intermediate- or distally-positioned helical coil portion acting as an electrode, for example.

An insulative sheath or other member **594**, **694**, **794**, **894** comprising non-conductive material can be disposed about the outer surface of the corewire **580**, **680**, **780**, **880**, helical coil(s) **584**, **884*a***, **884*b***, electrically-conductive polymer layer **686**, hypotube **788**, or braid to electrically insulate the components from one another and from surrounding body tissue when implanted. Suitable materials for the insulative sheath or other member **594**, **694**, **794**, **894** can include medical grade polymers, such as silicone and polyurethane, which can be engineered to create a desired degree of flexibility for bending during surgery. Suitable materials can also have a low coefficient of friction, such as PTFE, polyperfluoroalkoxy (PFA), fluorinated ethylene-propylene (FEP), polyethylenechlorotrifluoro-ehtylene (ECTFE), silicone rubber, polyurethane, and styrene-ethylene-butylene-styrene block polymer.

FIGS. **9-14** are enlarged schematic illustrations of distal end portions **962, 1062**, **1162**, **1262**, **1362**, **1462** of an example pacing guidewire's elongate body **950**, **1050**, **1150**, **1250**, **1350**, **1450**. The distal end portion of the elongate body can have a preformed shape **990**, **1090**, **1190**, **1290**, **1390**, **1490**, such as a pigtail shape (FIGS. **9-11**), a J-shape (FIGS. **12** and **13**), a V-shape (FIG. **14**) or other non-linear shape, prior to surgery to provide a relatively long, gentle bend that limits the risk of damage to delicate tissue (e.g., vessel walls, aortic or mitral valves, or ventricular walls) during introduction and positioning of the guidewire within a patient or to provide a region to conform to anatomical shapes (e.g., the ventricular apex). A prearranged loading tool can be included with the guidewire for straightening and facilitating introduction of its distal end portion into a guide catheter. As will be appreciated, the introduction of an elongate resilient bend can minimize the likelihood of trauma to the patient by transmitting forces applied to cardiac tissues and structures by the guidewire along a dispersed, radial path rather than along a

concentrated, longitudinal path via the guidewire's tip. The looping bend can also provide for a longer transition between the stiff support section of the guidewire and the softer atraumatic distal end portion. In an example, the distal end portion has relatively enhanced flexibility and low tip stiffness (e.g., 1g, 2g, 3g, 4g or 5g) such that the preformed shape can instantly curve into its unbiased shape upon discharge from the guide catheter.

To form the preformed biased shape **990**, **1090**, **1190**, **1290**, **1390**, **1490**, a corewire, a surrounding conductor, or both, can be constructed of a superelastic material, such as a nickel-titanium alloy, and can be manufactured in the biased shape to thus bias the elongate body **950**, **1050**, **1150**, **1250**, **1350**, **1450**. The distal end portion of the corewire, the surrounding conductor, or both, can optionally be shaped during a thermal shape setting process. As part of the process, the distal end portion(s) can be inserted into a sleeve that is shaped into a desired configuration. Heat can then be applied to the distal end portion(s) through the sleeve for a period of time. Once cooled and removed from the sleeve, the corewire, the surrounding conductor, or both, can be permanently imparted with the desired shape. Accordingly, although the elongate body **950**, **1050**, **1150**, **1250**, **1350**, **1450** can be reconfigured upon applying a suitable force thereon (e.g., straightened during insertion through a guide catheter), the thermal treatment of the corewire, the surrounding conductor, or both, can cause the distal end portion of the elongate body to resiliently return to its preformed configuration in the absence of forces.

As shown in the examples of FIGS. **9-14**, first and second electrodes **956**, **958**, **1056**, **1058**, **1156**, **1158**, **1256**, **1258**, **1356**, **1358**, **1456**, **1458** can be spaced apart along, and supported by, the preformed shape **990**, **1090**, **1190**, **1290**, **1390**, **1490**. Optionally, as shown in the example of FIG. **10**, third and fourth electrodes **1059**, **1061** can also be spaced along the preformed shape **1090** and can have the same polarity as the second electrode **1058** (via connection to the same conductor). The addition of the third and fourth electrodes **1059**, **1061** can increase the likelihood of electrode contact with heart wall tissue.

The pigtail shape **990**, **1090**, **1190** of FIGS. **9-11** can have a side height **982**, **1082**, **1182** of between about 20mm-40mm, can turn through more than 270 degrees, more than 360 degrees or more than 540 degrees, and can be composed of a corewire and one or more helical coils, for example. The present inventors have found that multiple nested loops (e.g., a first loop within a second loop) make it even less likely that the distal end portion of the guidewire can cause trauma to bodily tissue during its positioning. The corewire can be made from an electrically-conductive material and, alone or in combination with a first helical coil or other structure, can form one of the guidewire's elongate conductors. For example, as shown in FIG. **15**, a corewire **1580** can be electrically coupled to a first helical coil or first helical coil portion **1584*a*** to form an elongate conductor. A second helical coil or second helical coil portion can surround a portion of the corewire and, alone or in combination with another structure(s) (e.g., hypotube and/or braid), can form the second of the guidewire's conductors. As shown in FIG. **16**, first and second helical coils or helical coil portions **1684*a***, **1684*b*** can be longitudinally separated by a coil insulator **1679** positioned between a guidewire's two electrodes having opposite polarities.

Each helical coil or helical coil portion can include one or more filars and can be constructed from an appropriate formable material, such as but not limited to stainless steel, that is surrounded by insulation optionally applied with a lubricious coating on its exterior surface to facilitate advancement and retraction of the guidewire through the guide catheter. The use of a stainless steel material to form the helical coils can render them radiolucent. Accordingly, a portion of the helical coils can be applied with a radiopaque surface treatment (e.g., a platinum, palladium, gold, tantalum, or tungsten-based treatment) to render them highly visible under fluoroscopy.

The pigtail shape **990**, **1090**, **1190** of FIGS. **9-11** can optionally have a gradual reduction in cross-sectional diameter toward its distal end, and the radius of curvature of the pigtail shape can also decrease toward the distal end. This can

provide a resulting pacing guidewire that has adequate stiffness to be inserted into a heart and provides support for items delivered OTW (e.g., aortic valve implantation systems), while also having flexibly and resilience so that it can maintain at least one electrode in contact with a ventricular wall in the presence of factors such as the beating of the heart and patient movement, both of which can interrupt engagement between an electrode and the ventricular wall.

The preformed shape of the distal end portion of the guidewire's elongate body need not be constructed as a single plane structure. Rather, since the space within the left ventricle is multi-planar, the preformed shape **1390** of the distal end portion **1362** can be constructed as a multi-planar structure, as shown in FIG. **13**. The distal end portion **1362** can be non-coplanar relative to adjacent distal end portions or relative to the proximal or intermediate portions of the elongate body. In an example, the distal end portion **1362** is disposed at an angle **1392** relative to a plane containing the central axis of an intermediate portion **1364** of the elongate body, where the angle is between about 2 degrees and about 30 degrees.

FIGS. **17-19** are enlarged schematic illustrations of example electrode configurations designed to contact and stimulate heart tissue. A distal end portion **1762**, **1862**, **1962** of an elongate body **1750**, **1850**, **1950** can be provided with at least first and second electrodes **1756**, **1758**, **1856**, **1858**, **1956**, **1958** spaced apart by an insulative sheath or other member **1794**, **1894**, **1994**. The electrodes **1756**, **1758**, **1856**, **1858**, **1956**, **1958** can be electrically connected through or along the elongate body **1750**, **1850**, **1950** by first and second conductors to the proximal end portion of the elongate body. In an example, the first electrode **1756**, **1856**, **1956** can be provided at or near the distal end portion of the guidewire, and the second electrode **1758**, **1858**, **1958** can be spaced rearward (or more proximal) from the first electrode. Each electrode can beneficially be formed of platinum, carbon, iridium or titanium, for example, and its surface can optionally be treated using chemical, mechanical, or electrical and mechanical methods to improve resistance to

polarization or decrease the stimulation threshold. One or both electrodes can be radiopaque to assist in fluoroscopic location of the measurement site.

It is within the contemplation of the present pacing guidewires that there be no separate electrode structure and an exposed surface of a conductor in which the insulative sheath has been removed can be an electrode. The insulative sheath can be removed about the entire circumference of the conductor, forming a ring-shaped electrode surface, or only a portion of the insulative sheath can be removed circumferentially about the conductor, forming a semi-ring shaped electrode surface. Exposing a length of a conductor to allow it to be the electrode has the advantage of eliminating a connection between a separate electrode structure and the conductor.

In the example of FIG. **17**, first and second conductors **1752**, **1754** in the form of helical coils **1784*a***, **1784*b*** of differing diameters and insulated from one another prior to winding are shown. The first conductor **1752** can extend more distal than the second conductor **1754** and can electrically connect to a first electrode **1756**. The first electrode **1756** can comprise a cup-shaped element defining the leading tip of the guidewire. A portion(s) of the insulation covering the second conductor **1754** can be removed to form second, more proximal electrode(s) **1758**. In embodiments where multiple electrode contacts are connected to the same conductor, the electrode with the best tissue contact, as determined by a pacing system analyzer (PSA), can serve as the stimulating electrode. This configuration can allow for a decrease in stimulation threshold.

Alternatively, as shown in the example of FIG. **18**, a second, more proximal electrode **1858** can comprise a ring electrode spaced from a first, more distal electrode **1856**. The electrical connection between a second conductor **1854** and the ring electrode can be by means of a crimp ring. The crimp ring can have a length approximately one-half the axial length of the ring electrode. In effecting the connection of the second conductor **1854** to the second electrode **1858**, the distal end portion of the conductor can be brought out from the guidewire at a point

adjacent the distal end of the crimp ring. The conductor **1854** can be folded back toward the proximal end portion of the guidewire. The electrode **1858** can then be slipped over the guidewire and the crimp ring can clamp the end of the conductor **1854** therebetween. Upon installation of the electrode **1858**, the assembly can be dipped in a suitable adhesive material to fill the bore from which the conductor **1854** may be removed in bringing its distal end portion outwardly from the guidewire. The electrode **1858** can be formed with connector elements on its inner surface to receive the distal end portion of the conductor in a variety of other ways as well.

In the example of FIG. **19**, an outer surface of each of first and second electrodes **1956**, **1958** can be raised beyond an outer surface of the elongate body **1950**. Electrodes designed in this fashion can increase the chances of achieving intimate tissue-electrode contact resulting in lower pacing thresholds.

Interplay of example pacing guidewire and heart:

FIG. **20** is a schematic illustration of an example pacing guidewire **2048** positioned within a left ventricle **2016** of a heart **2004**. In this position, the guidewire **2048** can provide good support for the OTW delivery of elongate aortic valve treatment devices and can provide electrical stimuli to the left ventricle **2016** to induce and maintain cardiac ventricular tachycardia during medical procedures such as TAVI, TAVR and BV.

The guidewire **2048** can include an elongate body **2050** having an intermediate portion **2064** positioned within an aortic valve **2018** and a distal end portion **2062** extending into the left ventricle **2016**. The distal end portion **2062** can conceptually be separated into a first region **2096** configured to contact a ventricular wall **2001** on a first side of a ventricular apex **2003**, a second region **2097** configured to span across the apex **2003**, a third region **2098** configured to contact a ventricular wall **2005** on a second side of the apex **2003**, and/or a fourth region **2099** configured to curve away from the ventricular wall **2005** on the second side of the apex **2003**.

Electrode means conductively connected to the distal end portion **2062** of the elongate body **2050** can provide low resistant and low impedance electrical interfaces with bodily fluid and excitable tissue in contact with, or in the vicinity of, the electrode means. In the example shown, a first electrode **2056** is disposed on the fourth region **2099**, a second electrode **2058** is disposed on the third region **2098**, a third electrode **2059** is disposed on the second region **2097**, and a fourth electrode **2061** is disposed on the first region **2096**. The second, third and fourth electrodes **2058**, **2059**, **2061** can have an opposite polarity as the first electrode **2056**, and collectively, these electrodes can serve as the positive and negative poles during pacing and can be maintained in good electrical contact with the walls of the left ventricle **2016** directly or indirectly via blood or other fluid. By way of example, the first electrode **2056** can serve as the anode, and the second, third and fourth electrodes **2058**, **2059**, **2061** can serve as the cathode. The present inventors have found that advantageous (low) capture and pacing thresholds can be achieved when at least the cathode is in direct or near direct contact with heart tissue (e.g., wall tissue of the left ventricle).

Temporary pacing laboratory tests and animal trials:

The energy transmission to the heart provided by two electrodes positioned within a left ventricle was investigated not only in laboratory tests, but also in practical animal trials.

First animal trial:

Temporary pacing of a pig's heart using two electrodes positioned in the left ventricle was successfully performed with a fraction of the energy required to capture and pace the heart relative to using conventional temporary pacing, which, as shown in FIG. **1**, involves a femoral or jugular venous puncture to place a unipolar pacing lead (first electrode) in a right ventricle and a second electrode on a patient's skin.

The present inventors also discovered that substantially less energy is required to pace a pig's heart using two electrodes positioned in the left ventricle relative to using a first electrode positioned at the skin's surface or in the aorta and a second electrode positioned in the left ventricle, as the following findings show.

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| Negative Pole | Positive Pole | Capture Threshold |
|---|---|---|
| Guidewire having a fully exposed pigtail at its distal end portion positioned in left ventricle | Electrode pad on back | 7mA |
| Guidewire having a fully exposed pigtail at its distal end portion positioned in left ventricle | Electrode clamp attached to skin near femoral access point | 5.5mA |
| Guidewire having a fully exposed pigtail at its distal end portion positioned in left ventricle | Electrode needle in chest | 3.5mA |
| Guidewire having a fully exposed pigtail at its distal end portion positioned in aorta | Guidewire having a partially exposed straight distal end portion positioned at apex in left ventricle | 4.0mA |
| Guidewire having a partially exposed pigtail at its distal end portion positioned in aorta | Guidewire having a partially exposed straight distal end portion positioned at apex in left ventricle | 3.5mA |
| Guidewire having a partially exposed straight distal end portion positioned in left ventricle with no ventricular wall contact | Pacing lead having a distal electrode positioned at apex in left ventricle | 0.3mA |

Second animal trial:

Three embodiments of the present bipolar pacing guidewire were tested for capture threshold in two different locations—the apex and mid-left ventricle—

within a pig's heart. Rapid pacing ability and functionality during inflation of a 20mm Edwards-Sapien™ 3 heart valve delivery system (Edwards Lifesciences, Irvine, CA) were also tested. The primary objective was to demonstrate consistently acceptable rapid pacing capture thresholds and persistent pacing induced hypotension under a series of unique conditions and positions. Capture thresholds were evaluated with pacing guidewires positioned in the left ventricular apex and mid-cavity at a rate of 130bpm using both positive and negative polarity at the distal node. Rapid pacing ability was confirmed at 180bpm with balloon inflation.

Using the bipolar pacing guidewires, capture thresholds were 1.2 +/- 0.36mA when the wire was positioned at the left ventricular apex and 1.75 +/- 0.25mA when the wire was positioned in the left ventricle mid-cavity, out of contact with the apex. Rapid pacing at 180bpm was then successfully achieved with all pacing guidewires at 2x capture threshold (FIG. **21**). The Edwards-Sapien™ 3 heart valve delivery system was subsequently introduced and re-confirmed consistent rapid pacing ability at 2x capture threshold during delivery system inflation (FIG. **22**).

As a control, unipolar left ventricular pacing was tested in a second pig model using an Amplatz Super Stiff guidewire (Boston Scientific Corporation, Boston, MA) and ground using a 22gauge needle in subcutaneous tissue. The guidewire was insulated with a 5French AR1 diagnostic catheter. Capture threshold testing was repeated in the mid-cavity and left ventricular apical positions and rapid pacing at 180bpm.

In the control arm, capture thresholds were 6.0mA and 5.0mA with the Amplatz Super Stiff guidewire in the mid-cavity and left ventricular apical positions, respectively. Rapid pacing at 180bpm was also confirmed at 2x capture threshold in both positions.

Transfemoral TAVI, TAVR and BV procedures using example pacing guidewire:

FIG. **23** is a schematic illustration of a prosthetic aortic heart **2302** valve being implanted using an example pacing guidewire **2348**, and an optional closed

loop external pulse generator **2342**. The guidewire **2348** can be designed as both an OTW delivery wire (e.g., to reliably guide aortic valve delivery systems and implants to a desired site) and a bipolar pacing means, thereby obviating the need for a dedicated right ventricular pacing system, which has been conventionally used and is illustrated in FIG. **1**. The guidewire **2348** can be a one-time use disposable device and a proximal connector body can be designed to be compatible with a reusable external pulse generator **2342**.

As part of the valve implantation procedure, the guidewire **2348** can be inserted through a guide catheter that extends from a femoral artery **2322**, through an ascending aorta **2320**, and within the aortic valve **2318** of a patient. The guidewire **2348** can be advanced through the guide catheter until its distal end portion projects into a left ventricle **2316** and assumes a preformed bias (e.g., pigtail) shape **2390**. As shown, the guidewire **2348** can travel along an arcuate path made up of a ventricular wall **2301** on a first side of a ventricular apex **2303**, the ventricular apex **2303**, and a ventricular wall **2305** on a second side of the ventricular apex **2303** as it is advanced into the left ventricle. In one example, when the guidewire **2348** is fully advanced into the left ventricle **2316**, a first electrode **2356** can be positioned a spaced distance from the ventricular wall **2305** on the second side of the ventricular apex, a second electrode **2358** can be positioned against this ventricular wall **2305**, and the guide catheter can be removed from the patient.

Positioned as such within the left ventricle, the guidewire **2348** can be used to transmit electrical stimuli from the external pulse generator **2342** to the first and second electrodes **2356**, **2358** to induce and maintain cardiac ventricular tachycardia, thereby resulting in reduced cardiac output to allow balloon deployment in the aortic annulus without embolization from cardiac flow. The electrical stimuli can be sufficiently slow to capture the ventricular myocardium in a 1:1 manner, while being sufficiently fast to lower the systolic blood pressure to less than about 70 millimeters of mercury (mmHg) and the pulse pressure to less than

about 20mmHg. In some examples, the transmitted electrical stimuli can result in a current flow of 3.0mA or less between the first and second electrodes **2356**, **2358** (during full pacing) or 1.5mA or less between the first and second electrodes **2356**, **2358** (during initial capture) and ventricular rates of 120-220 beats per minute (bpm).

Medical procedures utilizing the pacing guidewire **2348** as a delivery and support means can then be performed on the heart while it is maintained in a state of ventricular tachycardia. For example, an introducer sheath **2326** can be inserted over the guidewire **2348** and into the ascending aorta **2320**, with a balloon catheter **2328**, having a dilatation balloon **2330** on its distal end portion, passed over the guidewire **2348** and through the sheath **2326**. A physician can locate a distal tip **2332** of the introducer sheath **2326** using a radiopaque marker(s) **2334**, for example, and the dilatation balloon can be expanded radially outward into contact with native aortic valve leaflets **2336** as part of a BV procedure. With information concerning the size of the particular aortic valve **2318**, the balloon **2330** can be chosen so that it expands outward and nominally compresses the aortic valve leaflets **2336** against the surrounding aortic walls **2338**.

The physician or operating room staff can then crimp the expandable prosthetic aortic heart valve **2302** over the dilatation balloon **2330**. With the prosthetic heart valve **2302** crimped over the balloon **2330**, the physician can once again advance the balloon catheter **2328** over the guidewire **2348** and through the introducer sheath **2326** until the prosthetic heart valve **2302** is located at the aortic annulus and between the native aortic leaflets **2336**. When the physician is satisfied with the positioning and rotational orientation of the prosthetic heart valve **2302**, the balloon **2330** can be expanded into good contact with the aortic annulus. Once the valve is properly implanted, the physician can deflate the balloon **2330** and withdraw the balloon catheter **2328** over the guidewire **2348**. The introducer sheath **2326** can then be withdrawn simultaneously with, or followed by, the guidewire **2348**.

The external pulse generator **2342** can optionally contain electronics and software necessary to detect certain electrophysiological responses to the electrical stimuli and then adjust the transmitted stimuli in a closed loop manner (i.e., control the functioning of a heart in accordance with information obtained about its mechanical state). The pulse generator **2342** may be designed specifically for temporary use as part of a system to perform TAVI, TAVR or BV in which the goal is to drop blood pressure and cardiac output below a prespecified level to allow for safe balloon deployment. When cardiac output is below the prespecified level for safe balloon deployment, an indicator light **2351** on the pulse generator **2342** can change from red to green.

The electrophysiological responses can, in some examples, be detected from an intra-arterial pressure monitor **2353** positioned in a central artery **2355** using an indwelling catheter that is an existing component of the medical procedure. Monitored pressure signals, such as systolic blood pressure or pulse pressure, can be processed using an algorithm and an electrical stimuli (pacing) rate can designed to achieve 1:1 ventricular capture in most patients, such as about 120bpm to 220bpm, can be calculated. If the pacing rate at any point leads to less than 1:1 capture of the ventricle (as monitored, for example, by the relationship between pacing frequency and systolic pressure rise), the pulse generator **2342** can decrease pacing frequency in order to capture the ventricle in a 1:1 fashion, then re-initiate the algorithm to increase pacing rate in order to meet the hemodynamic goals as stated above (systolic blood pressure less than about 70mmHg and pulse pressure less than about 20mmHg).

Closing notes and examples:

TAVI, TAVR, BV and TMVR procedures are occurring with increasing frequency throughout the world. Further commercialization and development of new and alternative devices to facilitate such procedures are only going to encourage this trend.

The present pacing guidewires and methods can minimize procedural times, obviate potential complications, and optimize outcomes in TAVI, TAVR, BV and TMVR procedures. For example, the pacing guidewires can be configured to provide good support for the OTW delivery of elongate treatment devices with less chance of perforation or other damage of vessels, the native aortic or mitral valve, or cardiac tissues through which the guidewires are inserted. Pacing electrodes, by being part of each guidewire and insulated from one another, can minimize the steps and risks of the valve procedures by obviating the need for an additional venous puncture for insertion of a dedicated right ventricular temporary pacing lead and can be ready for capture tests or pacing without a delivery system in place.

Laboratory and animal trials have proven the safety and efficacy of cardiac pacing using electrodes associated with the pacing guidewires as an alternative to the traditional approach of separate dedicated temporary pacing leads. The animal trials, for example, suggest capture thresholds on par with traditional temporary right ventricular pacing leads (but without the associated risks) and significantly lower capture thresholds than those seen with standard guidewires acting as a unipolar system in the left ventricle. Unlike standard guidewires, the present pacing guidewires do not require insulation in the form of an over-the-wire delivery device to function, and therefore threshold testing can be carried out immediately after placement. Furthermore, the mechanical properties of these pacing guidewires, including a pre-shaped tip, demonstrated no preliminary safety concerns during delivery of a balloon-expandable valve delivery system from a femoral artery to a native aortic valve.

The above Detailed Description includes references to the accompanying drawings, which form a part of the Detailed Description. The Detailed Description should be read with reference to the drawings. The drawings show, by way of illustration, specific embodiments in which the present pacing guidewires and methods can be practiced. These embodiments are also referred to herein as "examples."

The Detailed Description is intended to be illustrative and not restrictive. For example, the above-described examples (or one or more features or components thereof) can be used in combination with each other. Other embodiments can be used, such as by one of ordinary skill in the art upon reviewing the above Detailed Description. Also, various features or components have been or can be grouped together to streamline the disclosure. This should not be interpreted as intending that an unclaimed disclosed feature is essential to any claim. Rather, inventive subject matter can lie in less than all features of a particular disclosed embodiment. Thus, the following claim examples are hereby incorporated into the Detailed Description, with each example standing on its own as a separate embodiment:

In Example 1, a pacing guidewire can comprise an elongate body and at least first and second electrodes. The elongate body can extend from a proximal end portion to a distal end portion and can have an intermediate portion therebetween. The distal end portion can include a preformed bias shape. The elongate body can include a first elongate conductor extending from a proximal end portion to a distal end portion that is electrically connected to the first electrode, and a second elongate conductor, insulated from the first elongate conductor, extending from a proximal end portion to a distal end portion that is electrically connected to the second electrode. The at least first and second electrodes can be spaced apart on the preformed bias shape, with one of the electrodes serving as an anode and the other electrode servicing as a cathode.

In Example 2, the pacing guidewire of Example 1 can optionally further comprise third and fourth electrodes electrically connected to the second elongate conductor.

In Example 3, the pacing guidewire of Example 2 can optionally be configured such that each of the second, third and fourth electrode has a cylindrical shape and serves as the cathode. A collective length of the second, third and fourth electrodes can be 15mm or less, 12mm or less, or 10mm or less.

In Example 4, the pacing guidewire of any one of Examples 1 or 2 can optionally be configured such that the second electrode has a non-cylindrical, strip-like shape axially extending for a length between 5cm and 10cm, inclusive.

In Example 5, the pacing guidewire of any one or any combination of Examples 1-4 can optionally be configured such that at least one of the first and second elongate conductors is formed of two or more structures that are electrically connected.

In Example 6, the pacing guidewire of Example 5 can optionally be configured such that the two or more structures include a first structure in the form of a corewire and a second structure in the form of a helical coil.

In Example 7, the pacing guidewire of Example 5 can optionally be configured such that the two or more structures include a first structure in the form of a hypotube or a braid and a second structure in the form of a helical coil.

In Example 8, the pacing guidewire of Example 7 can optionally be configured such that the hypotube or the braid surrounds a portion of a corewire.

In Example 9, the pacing guidewire of any one or any combination of Examples 1-8 can optionally be configured such that the first elongate conductor is slidable relative to the second elongate conductor such that spacing between the first and second electrodes is adjustable.

In Example 10, the pacing guidewire of any one or any combination of Examples 1-9 can optionally be configured such that each of the first and second elongate conductors is at least partially in the form of a helical coil.

In Example 11, the pacing guidewire of Example 10 can optionally be configured such that the helical coil includes a single helically-wound flat wire.

In Example 12, the pacing guidewire of Example 11 can optionally further comprise insulation surrounding an outer surface of the helical coil.

In Example 13, the pacing guidewire of Example 12 can optionally be configured such that at least one of the first and second electrodes is an exposed, non-insulated portion of the helical coil.

In Example 14, the pacing guidewire of any one or any combination of Examples 1-13 can optionally be configured such that the preformed bias shape includes one or both of a V-shaped region or a pigtail-shaped region.

In Example 15, the pacing guidewire of Example 14 can optionally be configured such that the V-shaped region is configured to conform to a ventricular apex of a heart.

In Example 16, the pacing guidewire of Example 14 can optionally be configured such that the pigtail-shaped region turns through 540 degrees or more.

In Example 17, the pacing guidewire of any one or any combination of Examples 1-16 can optionally be configured such that the preformed bias shape is non-coplanar relative to the intermediate portion of the elongate body.

In Example 18, the pacing guidewire of any one or any combination of Examples 1-17 can optionally further comprise a connector body removably couplable to the proximal end portion of the elongate body and electrically couplable to the proximal end portions of the first and second elongate conductors.

In Example 19, the pacing guidewire of Example 18 can optionally be configured such that the connector body includes a seal member between a first terminal, electrically couplable with the first elongate conductor, and a second terminal, electrically couplable with the second elongate conductor.

In Example 20, the pacing guidewire of any one of Examples 18 or 19 can optionally be configured such that the connector body includes first and second pulse generator connector portions electrically couplable to the first and second

elongate conductors, the pulse generator connector portions being color-coded for identification of each conductor's polarity.

In Example 21, a left ventricular pacing guidewire can comprise an elongate body and first, second, third and fourth electrodes. The elongate body can extend from a proximal end portion to a distal end portion and can have an intermediate portion therebetween. The distal end portion can include a first region configured to contact a ventricular wall on a first side of a ventricular apex, a second region configured to span across the ventricular apex, a third region configured to contact a ventricular wall on a second side of the ventricular apex, and a fourth region configured to curve away from the ventricular wall on the second side of the ventricular apex. The first electrode can be disposed on the fourth region, and the second, third and fourth electrodes can be disposed on one of the first region, the second region or the third region. The elongate body can include a first elongate conductor extending from a proximal end portion to a distal end portion that is electrically connected to the first electrode, and a second elongate conductor, insulated from the first elongate conductor, extending from a proximal end portion to a distal end portion that is electrically connected to the second, third and fourth electrodes.

In Example 22, the left ventricular pacing guidewire of Example 21 can optionally further comprise a connector body removably couplable to the proximal end portion of the elongate body and electrically couplable to the proximal end portions of the first and second elongate conductors.

In Example 23, the left ventricular pacing guidewire of Example 22 can optionally be configured such that the connector body includes a seal member between a first terminal, electrically couplable with the first elongate conductor, and a second terminal, electrically couplable with the second elongate conductor.

In Example 24, the pacing guidewire of any one or any combination of Examples 1-23 can optionally be configured such that all elements or options recited are available to use or select from.

The scope of the present pacing guidewires should be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled. In the appended claims, the terms "including" and "in which" are used as the plain-English equivalents of the respective terms "comprising" and "wherein." Also in the following claims, the terms "including" and "comprising" are open-ended; that is, a guidewire that includes features or components in addition to those listed after such a term in a claim are still deemed to fall within the scope of that claim. Moreover, the terms "first," "second," "third," etc. in the following claims are used merely as labels, and such terms not intended to impose numerical requirements on their objects.

The Abstract is provided to allow the reader to quickly ascertain the nature of the technical disclosure. It is submitted with the understanding that it will not be used to interpret or limit the scope or meaning of the claims.

WHAT IS CLAIMED IS:

1. A pacing guidewire, comprising:

an elongate body having an outer diameter ranging from about 0.36mm (0.014in) to about 0.97mm (0.038in) and configured to receive and to support delivery of an elongate treatment device that is advanced over the pacing guidewire, the elongate body extending from a proximal end portion of the pacing guidewire to a distal end portion of the pacing guidewire and having an intermediate portion therebetween, the distal end portion including a preformed bias shape; and

at least first and second electrodes spaced apart on the preformed bias shape, one of the electrodes serving as an anode and the other electrode serving as a cathode for delivering pacing pulses to a heart of a patient while the elongate body supports delivery of the elongate treatment device to the heart of the patient,

the elongate body including a first elongate conductor, which extends from the proximal end portion to the distal end portion that is electrically connected to the first electrode, and a second elongate conductor, which is insulated from the first elongate conductor and extends from the proximal end portion to the distal end portion that is electrically connected to the second electrode.

2. The pacing guidewire of claim 1, further comprising third and fourth electrodes electrically connected to the second elongate conductor.

3. The pacing guidewire of claim 2, wherein each of the second, third and fourth electrodes has a cylindrical shape and serves as the cathode, and wherein a collective length of the second, third and fourth electrodes is 15mm or less.

4. The pacing guidewire of claim 1 or 2, wherein the second electrode has a non-cylindrical, strip-like shape axially extending for a length between 5cm and 10cm.



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5. The pacing guidewire of any one of claims 1 to 4, wherein the first elongate conductor is slidable relative to the second elongate conductor such that spacing between the first and second electrodes is adjustable.

6. The pacing guidewire of any one of claims 1 to 5, wherein at least one of the first elongate conductor and the second elongate conductor is formed of two or more structures that are electrically connected.

7. The pacing guidewire of claim 6, wherein the two or more structures include a first structure in the form of a corewire and a second structure in the form of a helical coil.

8. The pacing guidewire of claim 6, wherein the two or more structures include a first structure in the form of a hypotube or a braid and a second structure in the form of a helical coil.

9. The pacing guidewire of claim 8, wherein the hypotube or the braid surrounds a portion of a corewire.

10. The pacing guidewire of any one of claims 1 to 5, wherein each of the first elongate conductor and the second elongate conductor is at least partially in the form of a helical coil.

11. The pacing guidewire of claim 10, wherein the helical coil comprises a single helically-wound flat wire.

12. The pacing guidewire of claim 10 or 11, further comprising insulation surrounding an outer surface of the helical coil.

13. The pacing guidewire of claim 12, wherein at least one of the first and second electrodes is an exposed, non-insulated portion of the helical coil.



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14. The pacing guidewire of any one of claims 1 to 13, wherein the elongate body includes a V-shaped region proximal of a pigtail- or a J-shaped region.

15. The pacing guidewire of claim 14, wherein the V-shaped region is configured to conform to a ventricular apex of the heart.

16. The pacing guidewire of any one of claims 1 to 15, wherein the preformed bias shape turns through 540 degrees or more.

17. The pacing guidewire of any one of claims 1 to 16, wherein the preformed bias shape is non-coplanar relative to the intermediate portion of the elongate body.

18. The pacing guidewire of any one of claims 1 to 17, further comprising a connector body removably couplable to the proximal end portion of the elongate body and electrically couplable to the proximal end portions of the first and second elongate conductors.

19. The pacing guidewire of claim 18, wherein the connector body includes a seal member between a first terminal, electrically couplable with the first elongate conductor, and a second terminal, electrically couplable with the second elongate conductor.

20. The pacing guidewire of any one of claims 18 or 19, wherein the connector body includes first and second pulse generator connector portions electrically coupled to the first and second elongate conductors, the pulse generator connector portions being color-coded for identification of each conductor's polarity.

21. A left ventricular pacing guidewire, comprising:

an elongate body having an outer diameter ranging from about 0.36mm (0.014in) to about 0.97mm (0.038in), and configured to receive and to support delivery of an elongate



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treatment device that is advanced over the pacing guidewire, the elongate body extending from a proximal end portion of the pacing guidewire to a distal end portion of the pacing guidewire and having an intermediate portion therebetween, the distal end portion including a first region configured to contact a first ventricular wall of a heart on a first side of a ventricular apex, a second region configured to span across the ventricular apex, a third region configured to contact a second ventricular wall on a second side of the ventricular apex, and a fourth region configured to curve away from the second ventricular wall on the second side of the ventricular apex;

a first electrode disposed on the fourth region and spaced from the first and second ventricular walls; and

a second electrode, a third electrode and a fourth electrode disposed on one of the first region, the second region or the third region,

the elongate body including a first elongate conductor, which extends from a proximal end portion to a distal end portion that is electrically connected to the first electrode, and a second elongate conductor, which is insulated from the first elongate conductor and extends from a proximal end portion to a distal end portion that is electrically connected to the second, third and fourth electrodes.

22. The left ventricular pacing guidewire of claim 21, further comprising a connector body removably couplable to the proximal end portion of the elongate body and electrically couplable to the proximal end portions of the first and second elongate conductors.

23. The left ventricular pacing guidewire of claim 22, wherein the connector body includes a seal member between a first terminal, electrically couplable with the first elongate conductor, and a second terminal, electrically couplable with the second elongate conductor.

24. A left ventricular guidewire, comprising:

means for concurrently supporting delivery of an aortic valve treatment device and for inducing and maintaining cardiac ventricular tachycardia,



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wherein the means includes insulated anode and cathode poles positioned on a distal pigtail-shaped region such that a first pole is positionable away from a ventricular wall of a heart during pacing and a second pole is positionable in contact with the ventricular wall during pacing,

and wherein the pigtail-shaped region transmits applied insertion forces along a dispersed, radial path.

25. Use of a bipolar pacing guidewire for performing a medical procedure on a heart:

wherein a distal end portion of the bipolar pacing guidewire is for advancing into a left ventricle of a patient's heart, and for positioning first and second electrodes against or spaced from a left ventricular wall; and

wherein electrical stimuli are for transmitting through the guidewire to the first and second electrodes for inducing and maintaining cardiac ventricular tachycardia for performing said medical procedure.

26. The use of claim 25, wherein the distal end portion of the bipolar pacing guidewire includes a resiliently deformable, pre-formed curved shape for advancing into the left ventricle.

27. The use of claim 26, wherein the pre-formed curved shape includes a pigtail-shaped region that turns through 540 degrees or more, and wherein the first and second electrodes are spaced apart on the turns.

28. The use of any one of claims 25 to 27, wherein the first electrode is for positioning a spaced distance from the left ventricular wall and the second electrode is for positioning against the left ventricular wall.

29. The use of claim 28, wherein the first electrode is an anode and the second electrode is a cathode.



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30. The use of any one of claims 25 to 27, wherein the first electrode is for positioning against a first portion of the left ventricular wall on a first side of a ventricular apex and the second electrode is for positioning against a second portion of the left ventricular wall on a second side of the ventricular apex.

31. The use of any one of claims 25 to 30, wherein said electrical stimuli are for transmission through a first elongate conductor electrically connected to the first electrode and for transmission through a second elongate conductor electrically connected to the second electrode.

32. The use of claim 31, wherein said electrical stimuli for transmission through the first elongate conductor includes electrical stimuli for transmission through a corewire and a helical coil.

33. The use of claim 31, wherein said electrical stimuli for transmission through the second elongate conductor includes electrical stimuli for transmission through a hypotube or a braid and a helical coil.

34. The use of any one of claims 25 to 33, wherein said electrical stimuli for transmission to the first and second electrodes includes a current flow of 4.0mA or less between the electrodes.

35. The use of claim 34, wherein said electrical stimuli for transmission to the first and second electrodes includes generating a current flow of 3.0mA or less between the electrodes.

36. The use of any one of claims 25 to 35, wherein cardiac ventricular tachycardia includes ventricular rates of 120-220 bpm and lowering of the patient's blood pressure.

37. The use of any one of claims 25 to 36, wherein the medical procedure is selected from the group consisting of percutaneous transcatheter aortic valve implantation (TAVI), transcatheter



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aortic valve replacement (TAVR), balloon valvuloplasty (BV) and transcatheter mitral valve replacement (TMVR).

38. The use of claim 37, wherein the medical procedure is BV and wherein a balloon catheter is provided for placing over the pacing guidewire for positioning a dilatation balloon, at a distal end portion of the balloon catheter, within a native aortic valve, wherein the dilatation balloon is for radially expanding for urging a prosthetic heart valve into contact with the native aortic valve.

39. The use of claim 37, wherein the medical procedure is BV and wherein a balloon catheter is provided for placing over the pacing guidewire for positioning a dilatation balloon, at a distal end portion of the balloon catheter, within a native aortic valve, wherein the dilatation balloon is for urging a prosthetic heart valve into contact with the native aortic valve.

40. The use of claim 38 or 39, wherein the electrical stimuli for transmission through the guidewire is adjustable once the dilatation balloon is deflated.

41. The use of claim 37, wherein the medical procedure is BV and wherein a balloon catheter is provided for placing over the pacing guidewire for positioning a dilatation balloon, at a distal end portion of the balloon catheter, within a native mitral valve, wherein the dilatation balloon is for urging a prosthetic heart valve into contact with the native mitral valve.

42. The use of any one of claims 25 to 41, wherein the electrical stimuli transmitted through the guidewire are adjustable based on an electrophysiological response.

43. The use of claim 42, wherein the electrophysiological response is for sensing if less than 1:1 capture of the left ventricle exists.



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44. The use of claim 42, wherein the electrophysiological response comprises the patient's systolic blood pressure or pulse pressure.

45. The use of claim 42, wherein the electrical stimuli transmitted through the guidewire is increasable if the patient's systolic blood pressure is less than 70mmHg or the pulse pressure is less than 20mmHg.

46. The use of any one of claims 25 to 45, further comprising a connector body for removably coupling to a proximal end portion of the bipolar pacing guidewire, and first and second terminals of the connector body are for electrically coupling to first and second elongate conductors respectively associated with the first and second electrodes.

47. The use of claim 46, further wherein shorting is prevented between the first and second elongate conductors.

48. Use of the pacing guidewire of any one of claims 1 to 20 for aiding in percutaneous replacement of a heart valve.

49. The use of claim 48, wherein said percutaneous replacement is percutaneous transcatheter aortic valve implantation (TAVI), transcatheter aortic valve replacement (TAVR), balloon valvuloplasty (BV) or transcatheter mitral valve replacement (TMVR).

50. Use of the left ventricular pacing guidewire of any one of claims 21 to 23 for transmitting electrical stimuli to a patient's heart and for guiding and supporting over-the-wire (OTW) delivery of elongate treatment devices within the heart.

51. The pacing guidewire of claim 1, wherein the first and second electrodes are spaced apart on the preformed bias shape such that a portion of the first electrode is positionable away from a



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ventricular wall of the heart during pacing and the second electrode is positionable in contact with the ventricular wall during pacing.

52. Use of the pacing guidewire of any one of claims 1 to 20 in a medical procedure selected from the group consisting of percutaneous transcatheter aortic valve implantation (TAVI), transcatheter aortic valve replacement (TAVR), balloon valvuloplasty (BV) and transcatheter mitral valve replacement (TMVR).

53. Use of the left ventricular pacing guidewire of any one of claims 21 to 23 for a medical procedure selected from the group consisting of percutaneous transcatheter aortic valve implantation (TAVI), transcatheter aortic valve replacement (TAVR), balloon valvuloplasty (BV) and transcatheter mitral valve replacement (TMVR).



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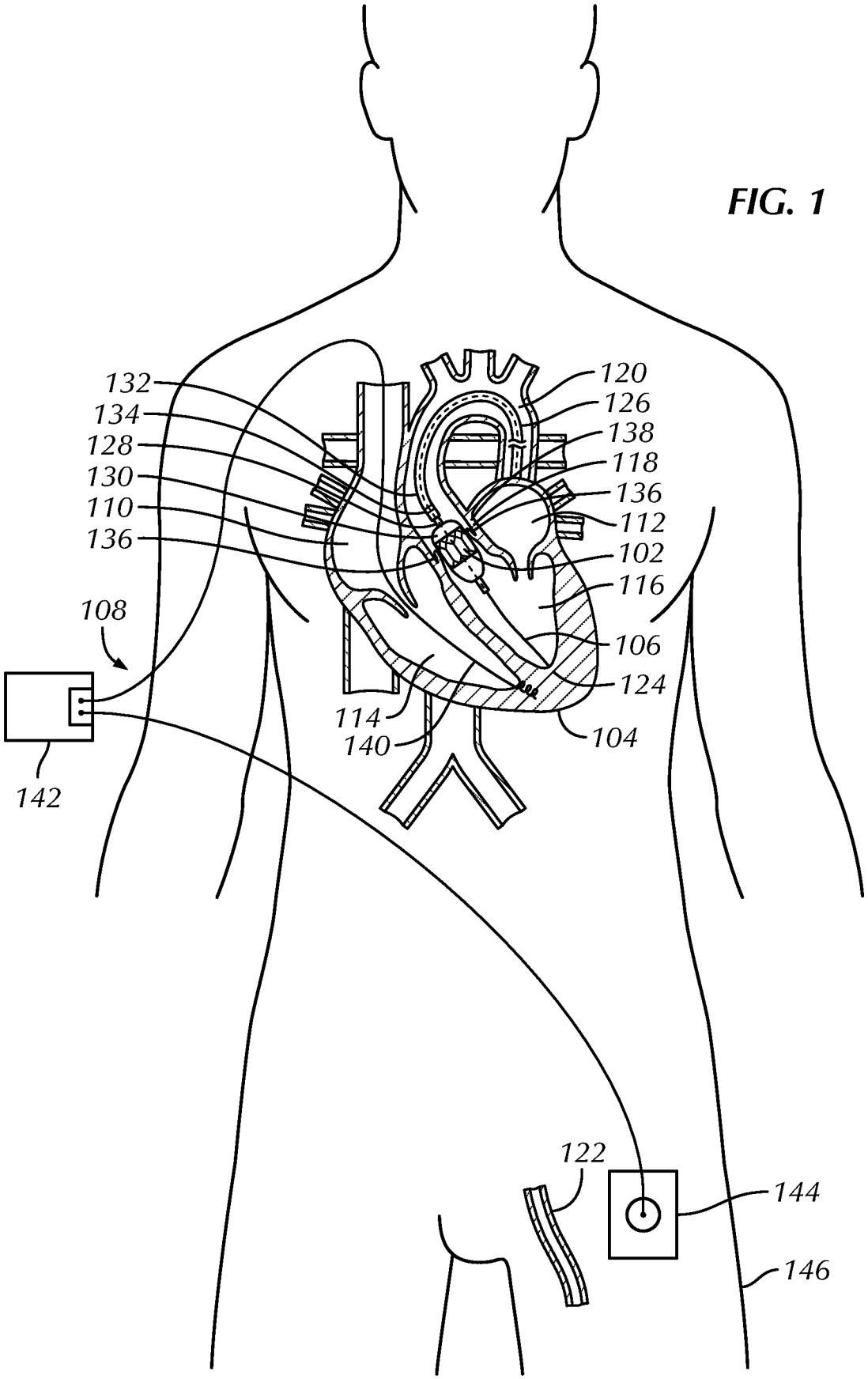
FIG. 1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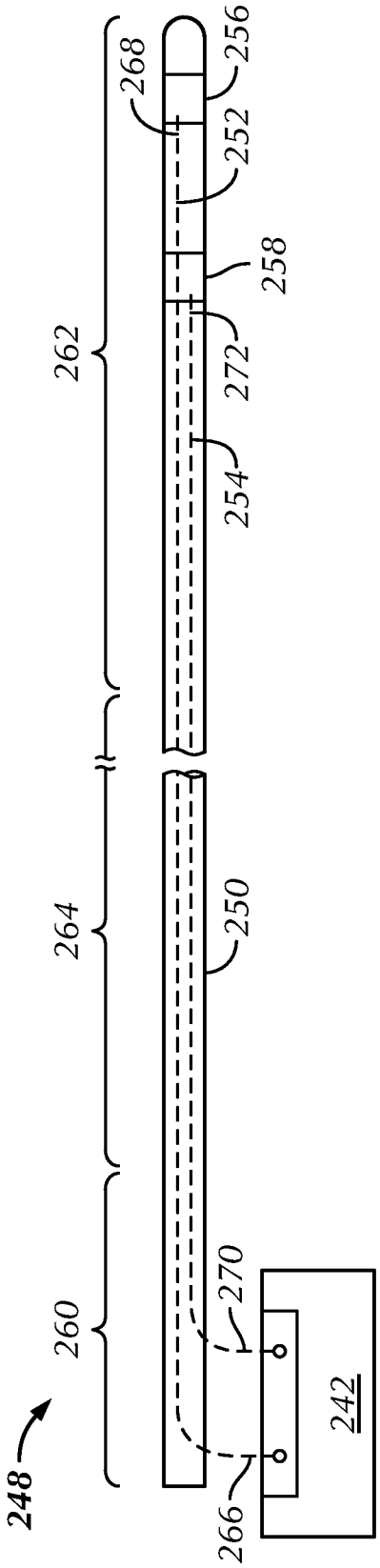
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FIG. 2

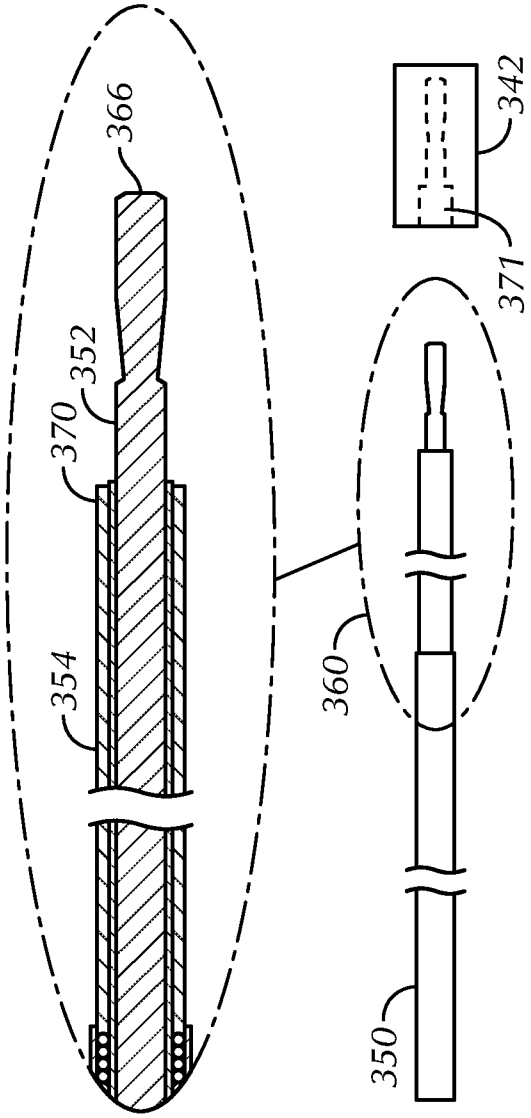
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FIG. 3

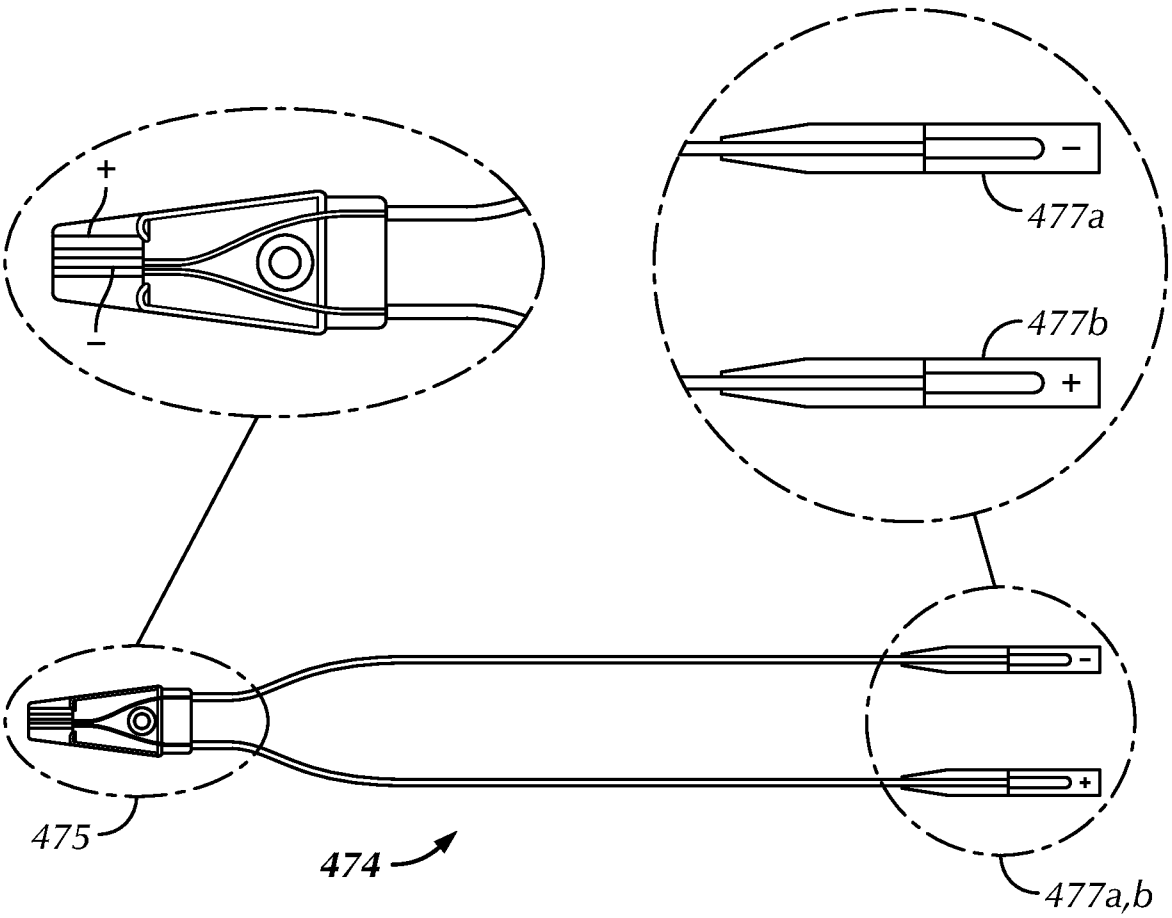


FIG. 4

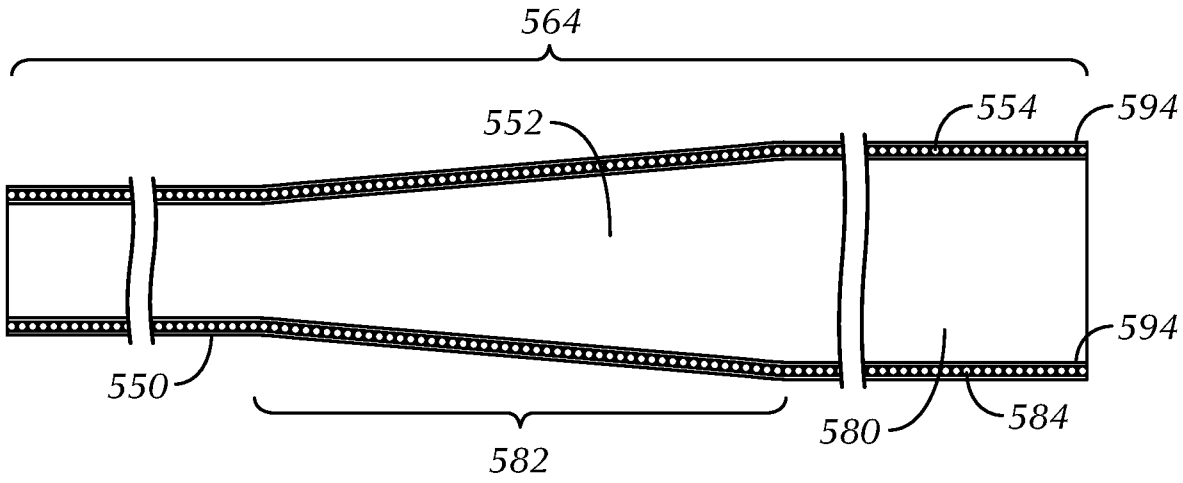
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FIG. 5

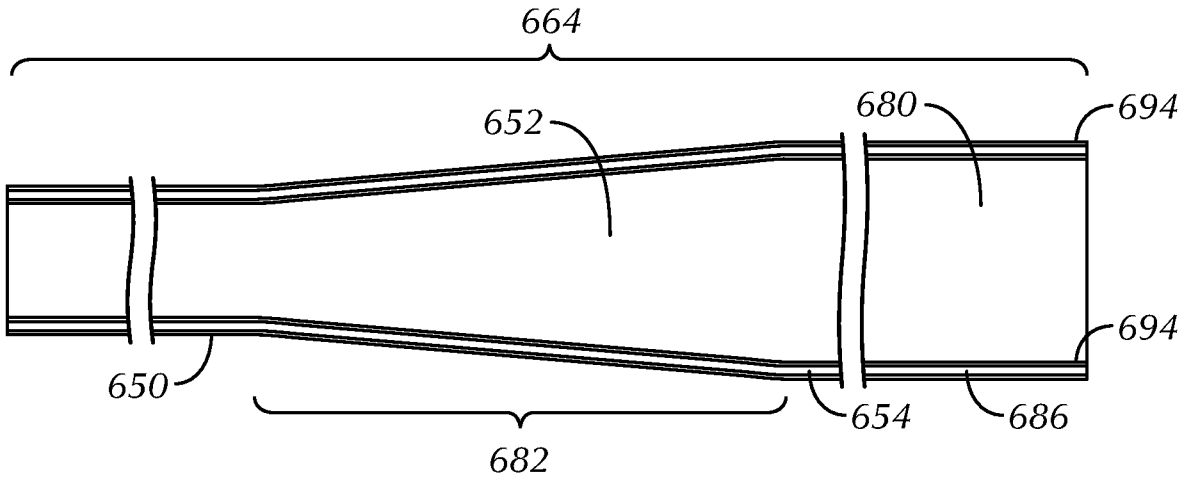
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FIG. 6

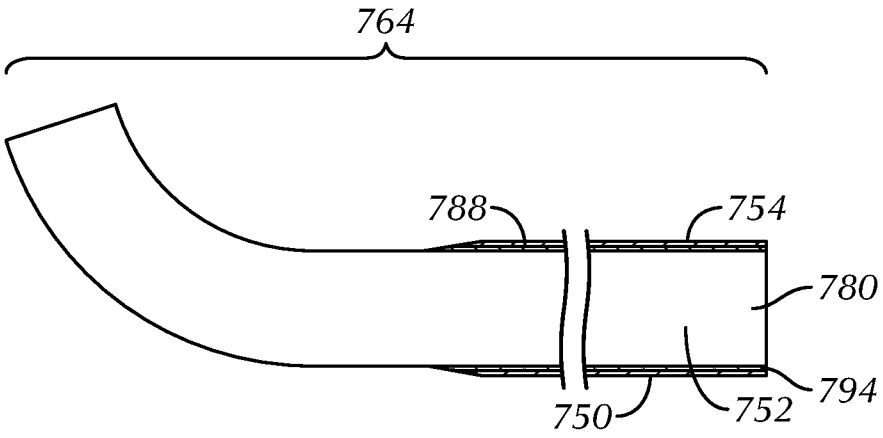
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FIG. 7

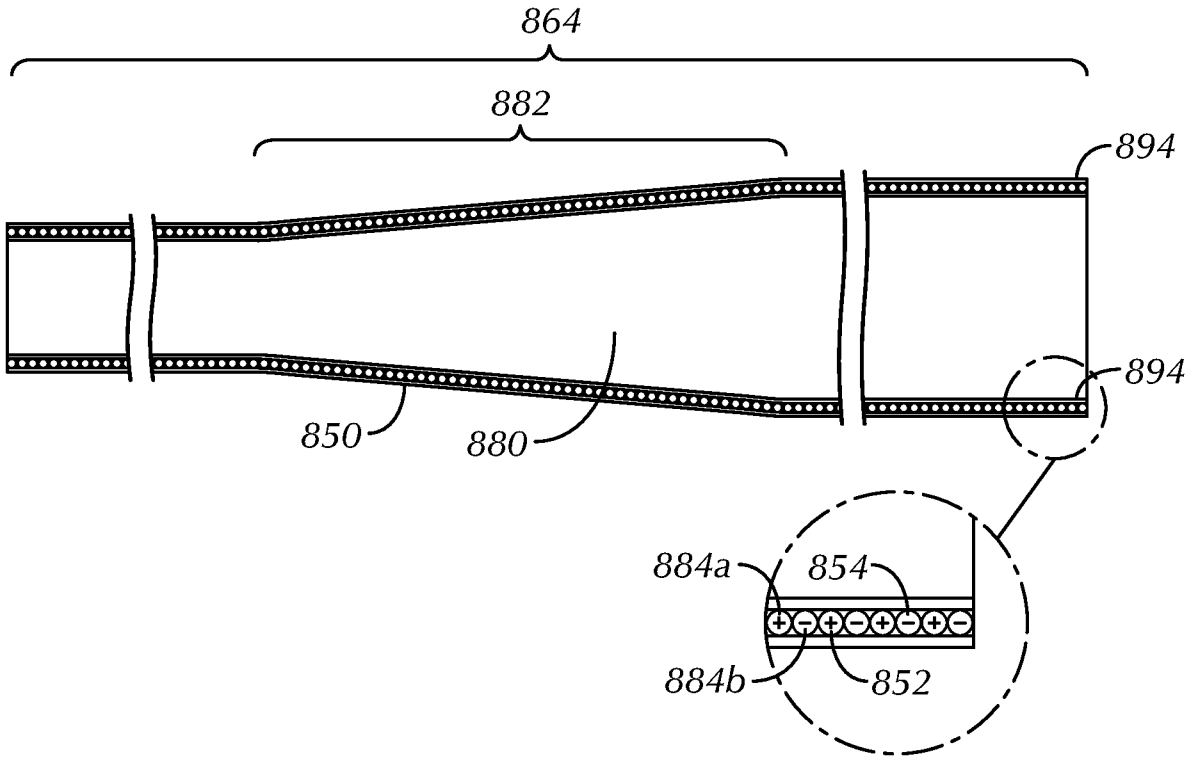
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FIG. 8

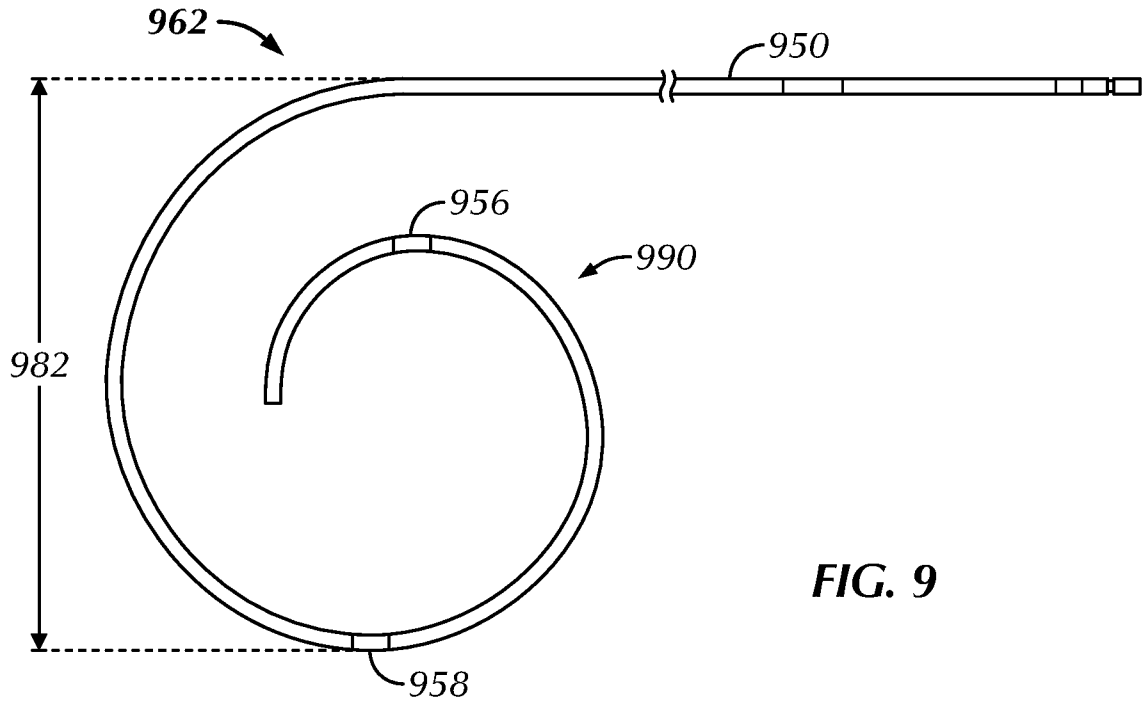
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FIG. 9

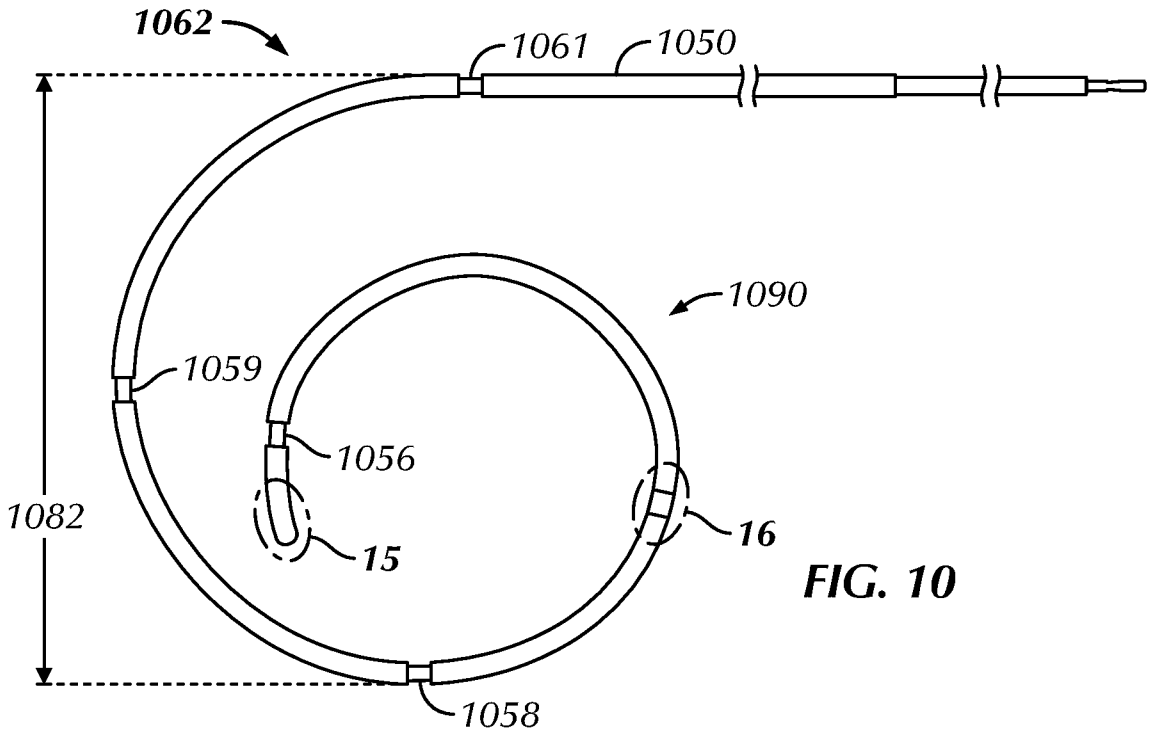
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FIG. 10

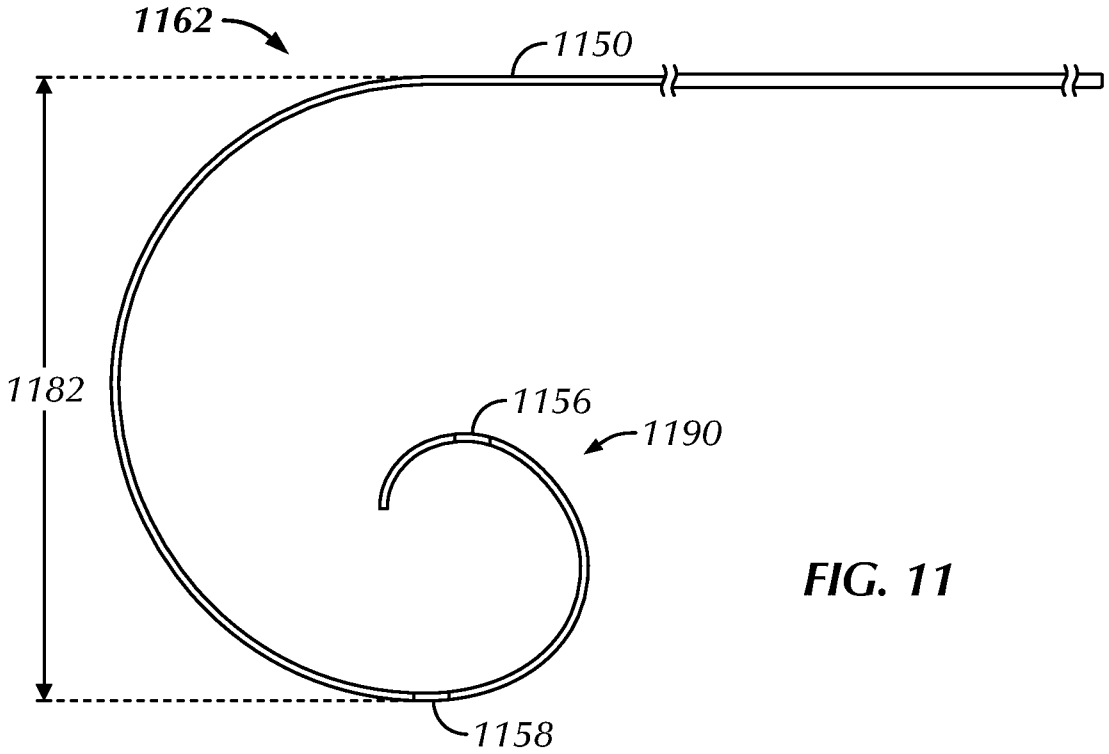


FIG. 11

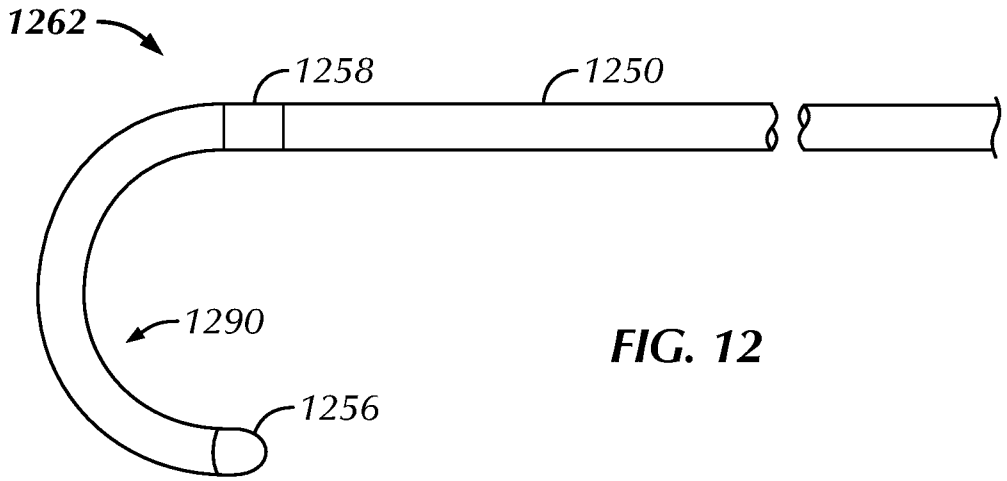


FIG. 12

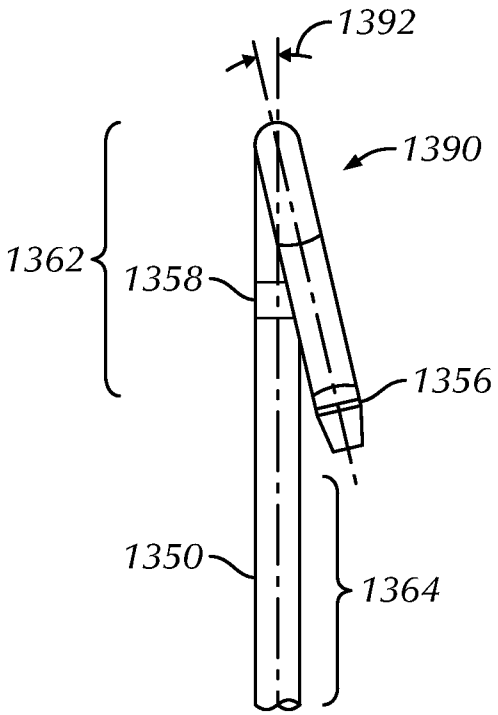


FIG. 13

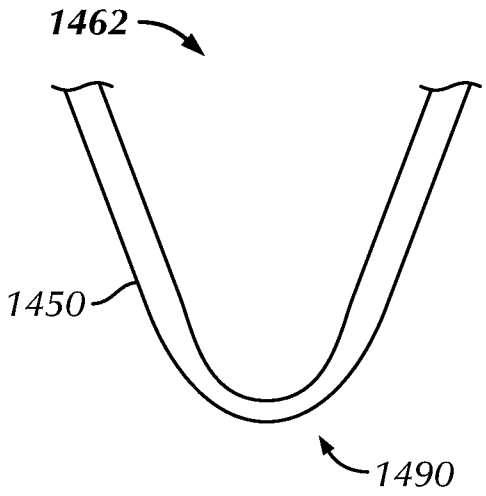


FIG. 14

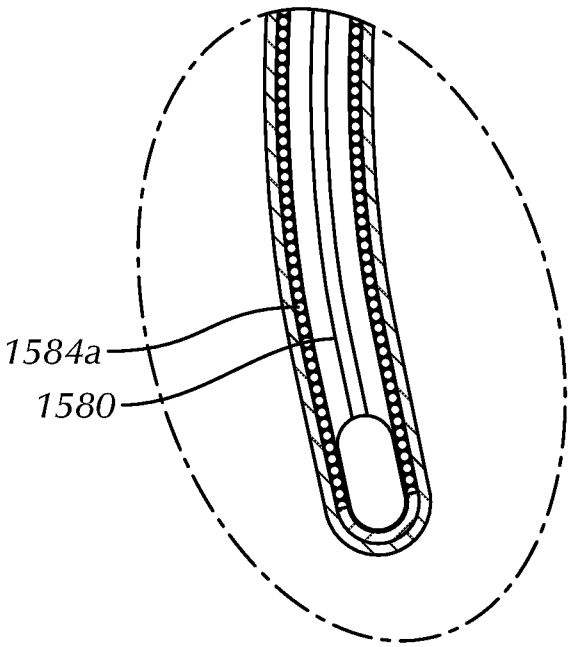


FIG. 15

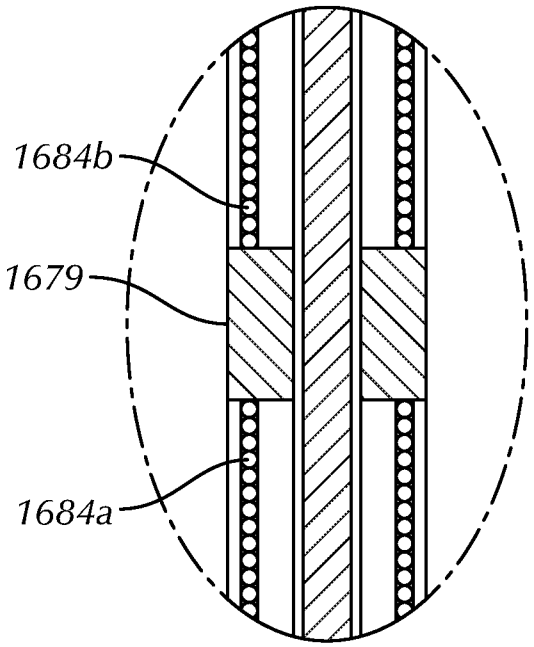


FIG. 16

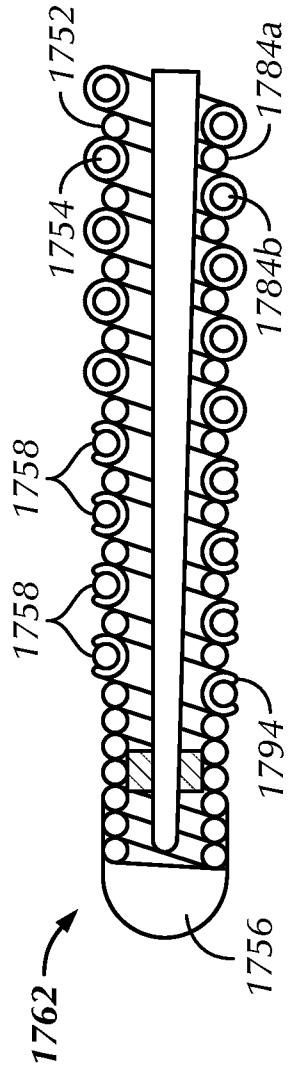


FIG. 17

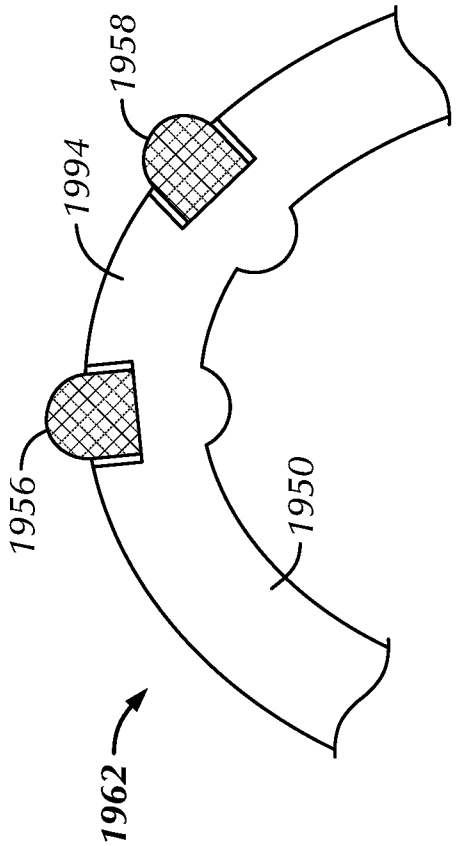


FIG. 19

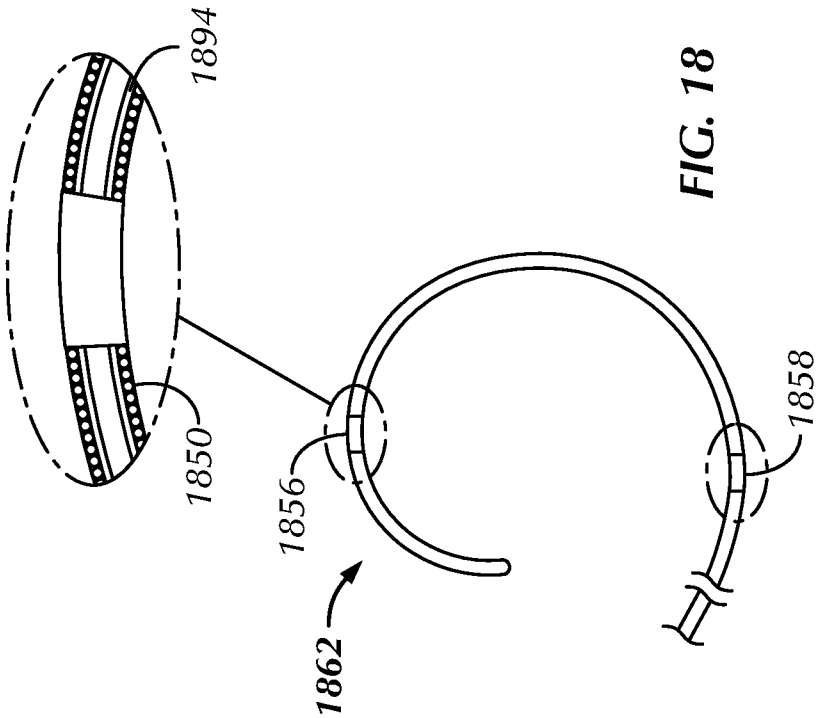


FIG. 18

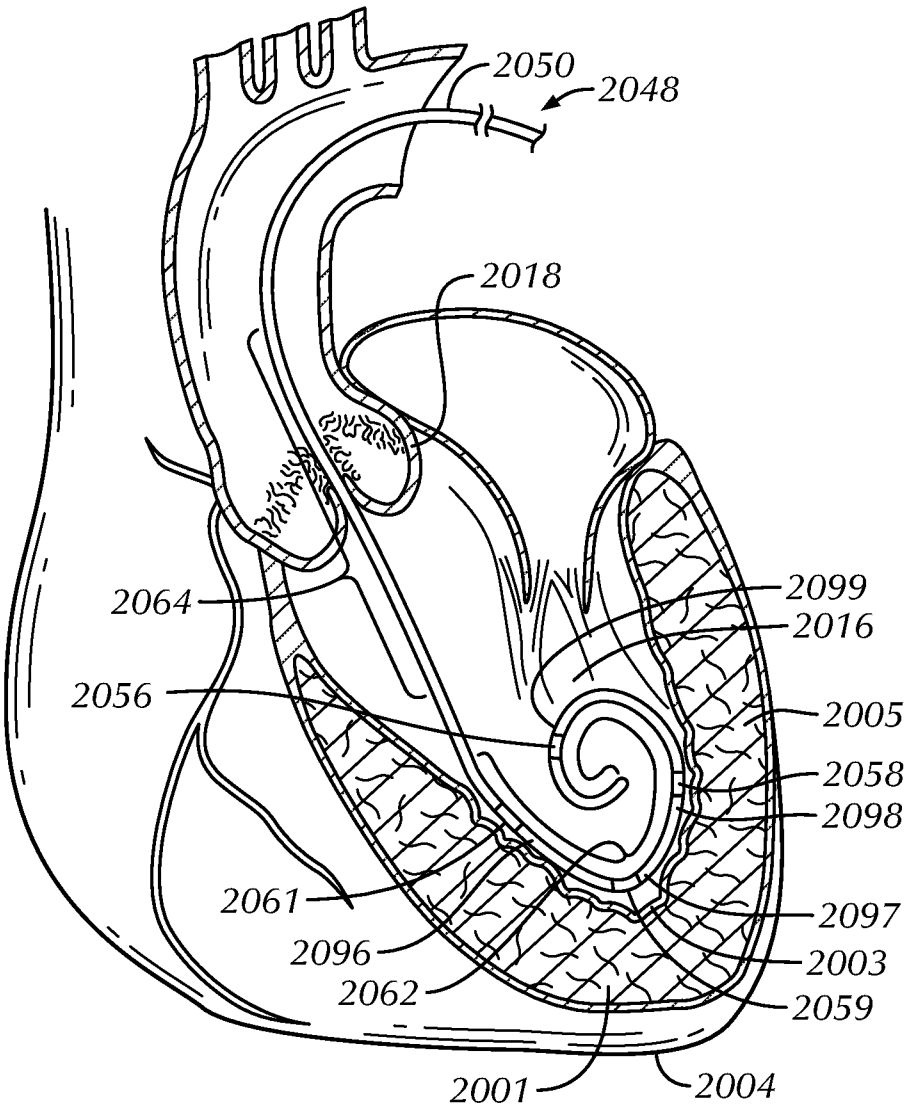
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FIG. 20

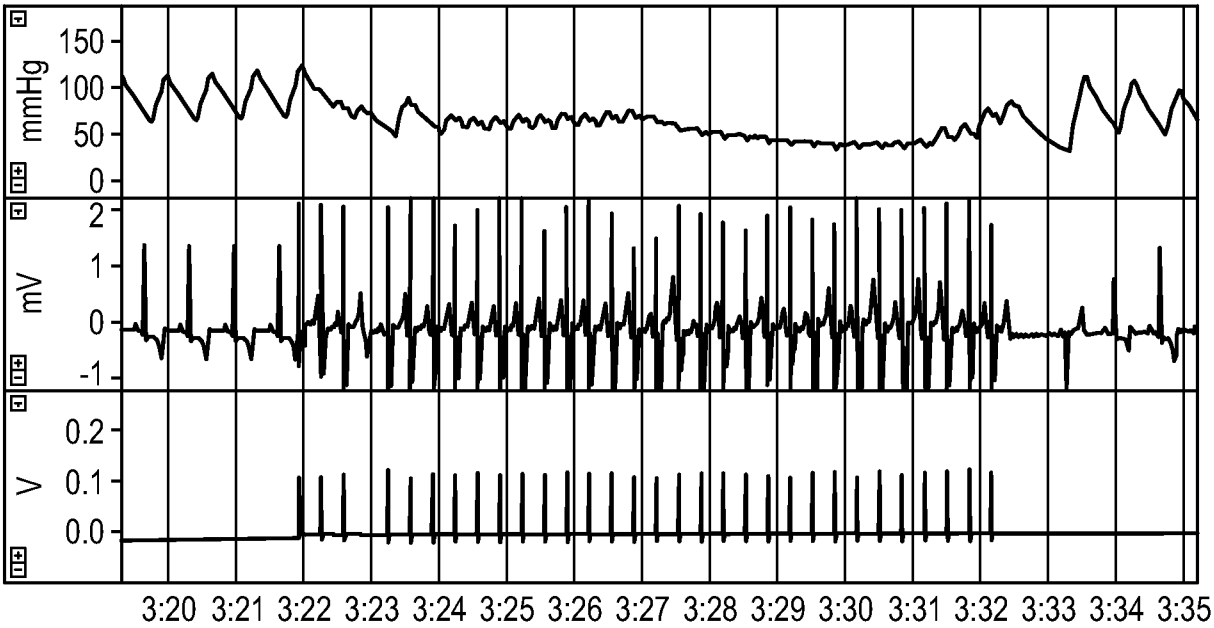
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FIG. 21

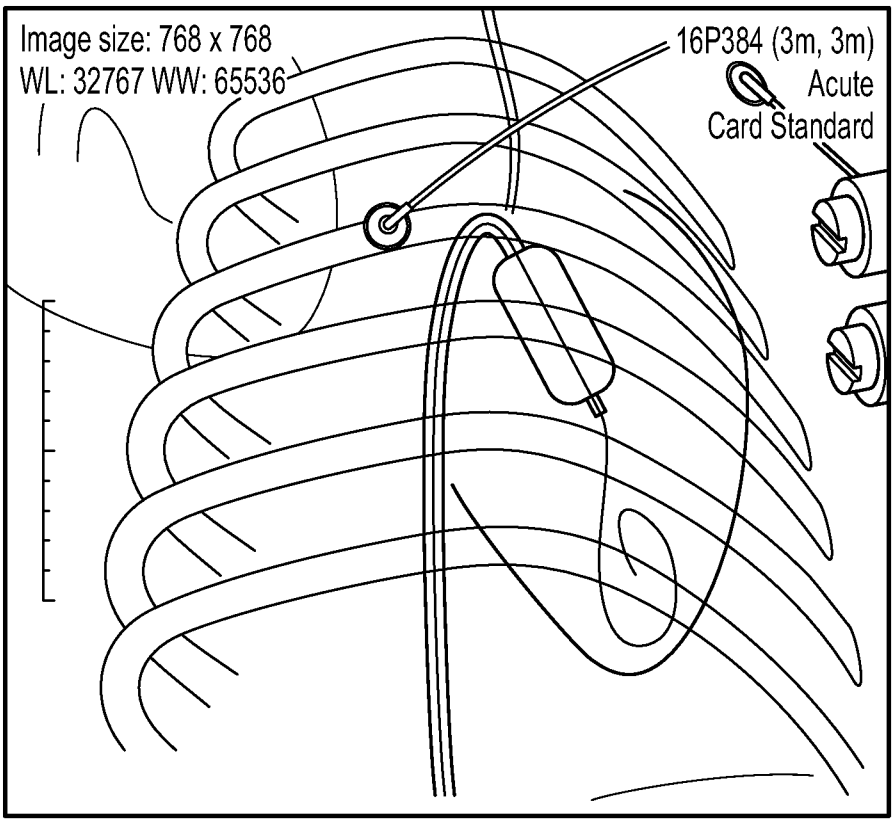
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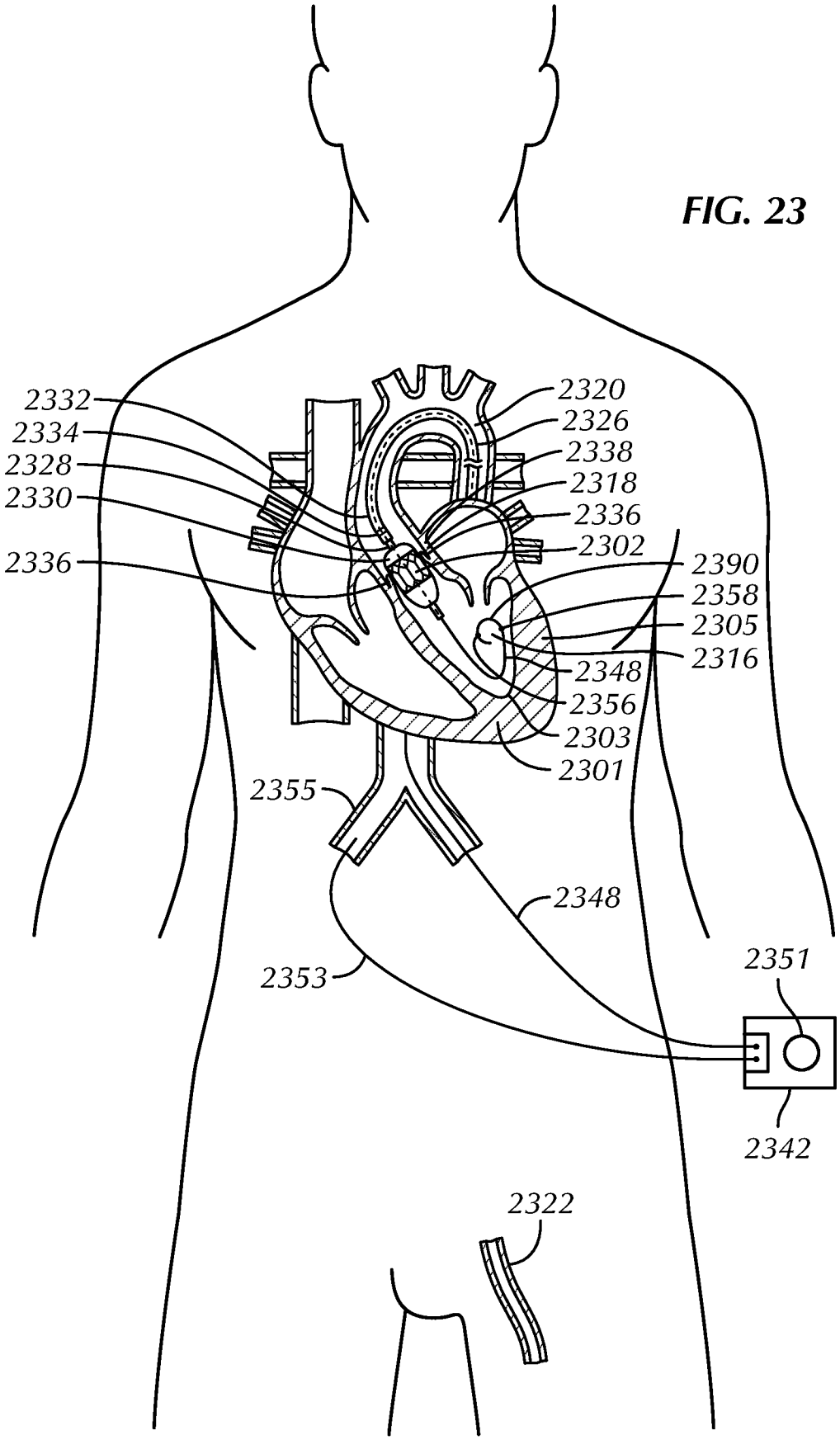
FIG. 22

FIG. 23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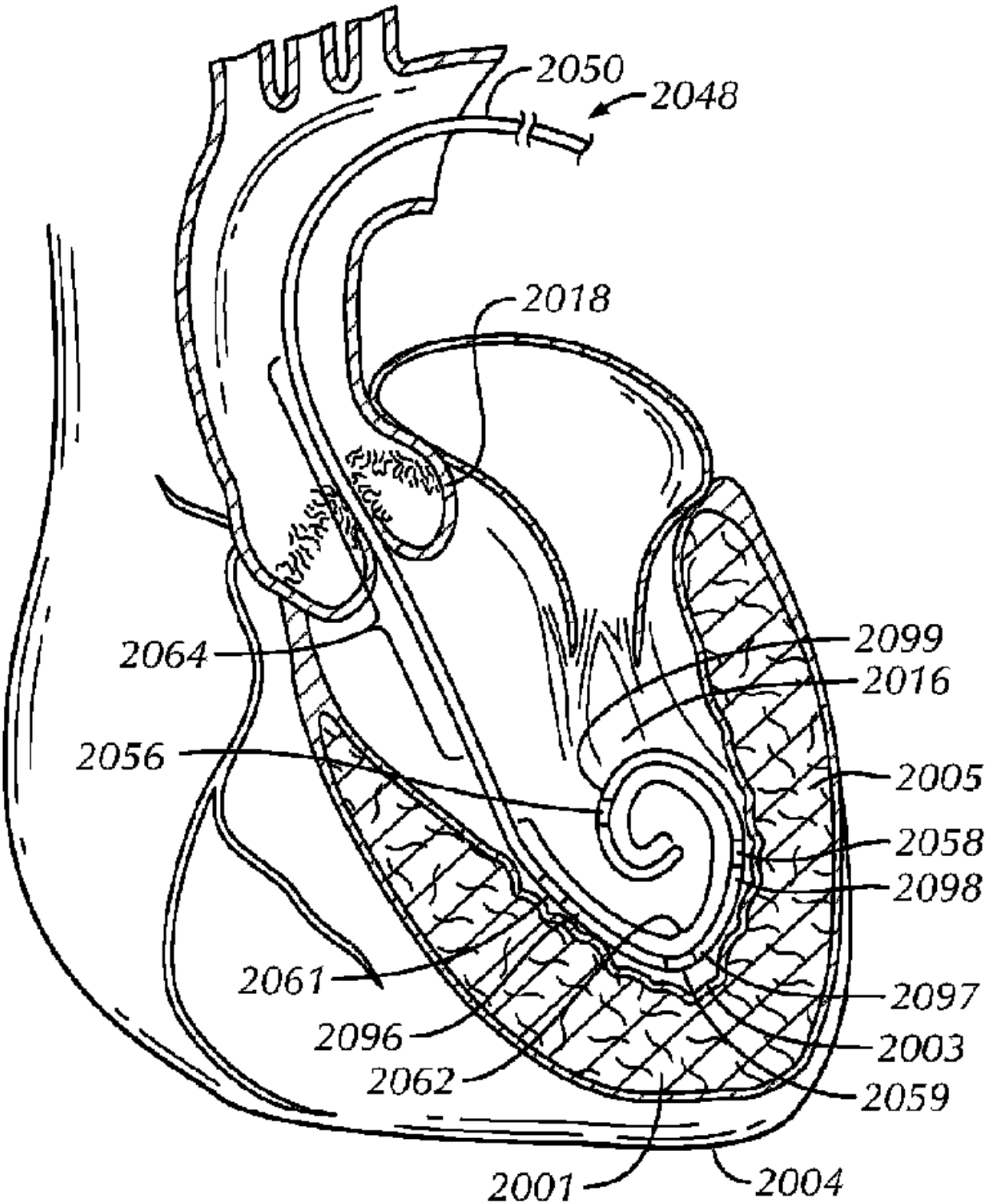
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