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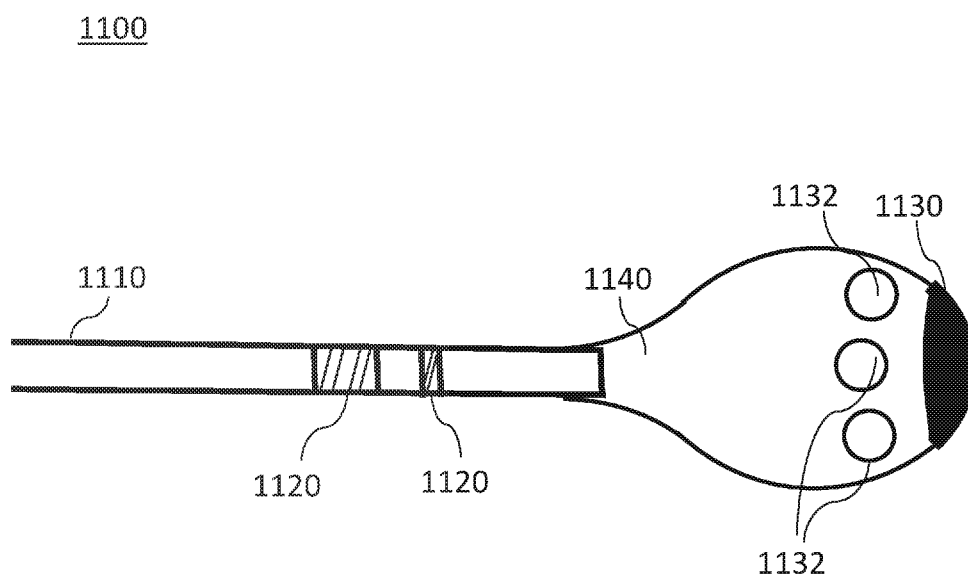


FIG. 11

(57) Abstract: Systems, devices, and methods for electroporation ablation therapy are disclosed, with the system including a pulse waveform signal generator for medical ablation therapy, and an endocardial ablation device includes an inflatable member and at least one electrode for focal ablation pulse delivery to tissue. The signal generator may deliver voltage pulses to the ablation device in the form of a pulse waveform. The system may include a cardiac stimulator for generation of pacing signals and for sequenced delivery of pulse waveforms in synchrony with the pacing signal.



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SYSTEMS, APPARATUSES, AND METHODS FOR VENTRICULAR FOCAL ABLATION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/557,390, filed on September 12, 2017, the disclosure of which is hereby incorporated by reference in its entirety.

BACKGROUND

[0002] The generation of pulsed electric fields for tissue therapeutics has moved from the laboratory to clinical applications over the past two decades, while the effects of brief pulses of high voltages and large electric fields on tissue have been investigated for the past forty years or more. Application of brief high DC voltages to tissue may generate locally high electric fields typically in the range of hundreds of volts per centimeter that disrupt cell membranes by generating pores in the cell membrane. While the precise mechanism of this electrically-driven pore generation or electroporation continues to be studied, it is thought that the application of relatively brief and large electric fields generates instabilities in the lipid bilayers in cell membranes, causing the occurrence of a distribution of local gaps or pores in the cell membrane. This electroporation may be irreversible if the applied electric field at the membrane is larger than a threshold value such that the pores do not close and remain open, thereby permitting exchange of biomolecular material across the membrane leading to necrosis and/or apoptosis (cell death). Subsequently, the surrounding tissue may heal naturally.

[0003] While pulsed DC voltages may drive electroporation under the right circumstances, there remains an unmet need for thin, flexible, atraumatic devices that effectively deliver high DC voltage electroporation ablation therapy selectively to endocardial tissue in regions of interest while minimizing damage to healthy tissue.

SUMMARY

[0004] Described here are systems, devices, and methods for ablating tissue through irreversible electroporation. Generally, an apparatus for delivering a pulse waveform to tissue

may include a catheter shaft defining a longitudinal axis. An inflatable member may be coupled to a distal end of the catheter shaft. The inflatable member may have an outer surface including a set of electrically conductive portions. A first set of electrodes may be formed on a surface of the catheter shaft. A second set of electrodes may be formed distal to the first set of electrodes on the surface of the catheter shaft. The second set of electrodes may be electrically coupled to the outer surface of the inflatable member and electrically isolated from the first set of electrodes.

[0005] In some embodiments, an apparatus may include a catheter shaft defining a longitudinal axis. An inflatable member may be coupled to a distal end of the catheter shaft. A first set of electrodes may be formed on a surface of the catheter shaft. A second electrode may be formed on the inflatable member and electrically isolated from the first set of electrodes.

[0006] In some embodiments, an apparatus may include a catheter shaft defining a longitudinal axis. An inflatable member may be coupled to a distal end of the catheter shaft. A first set of electrodes may be formed on the inflatable member and disposed proximal to an equatorial plane of the inflatable member. A second set of electrodes may be formed on the inflatable member and disposed distal to the equatorial plane of the inflatable member. The second set of electrodes may be electrically isolated from the first set of electrodes.

[0007] In some embodiments, a system may include a signal generator configured for generating a pulse waveform. An ablation device may be coupled to the signal generator and configured for receiving the pulse waveform. The ablation device may include a handle, a catheter shaft defining a longitudinal axis, and an inflatable member coupled to a distal end of the catheter shaft. The inflatable member may have an outer surface including a set of electrically conductive portions. A first set of electrodes may be formed on a surface of the catheter shaft. A second set of electrodes may be formed distal to the first set of electrodes on the surface of the catheter shaft. The second set of electrodes may be electrically coupled to the outer surface of the inflatable member and electrically isolated from the first set of electrodes.

[0008] In some embodiments, an apparatus may include a catheter shaft defining a longitudinal axis. An annular inflatable member may be coupled to a distal end of the catheter shaft. The inflatable member may define an annular inflatable member lumen therethrough. A first electrode may be disposed on a distal end of the annular inflatable member. The first

electrode may have a substantially planar portion. A second electrode may extend from, and be distal to, the annular inflatable member lumen and be spaced apart from the first electrode.

[0009] In some embodiments, the first set of electrodes may have a polarity opposite to a polarity of the second set of electrodes during delivery of a pulse waveform. In some embodiments, the first set of electrodes may have a polarity opposite to the polarity of the second electrode during delivery of a pulse waveform. In some embodiments, the first set of electrodes may have a polarity opposite to the polarity of the second set of electrodes during delivery of the pulse waveform.

[0010] In some embodiments, the catheter shaft may include a deflectable portion formed between the first set of electrodes and the second set of electrodes. The deflectable portion may be configured for deflecting a portion of the catheter including the second set of electrodes and the inflatable member up to about 210 degrees relative to the longitudinal axis. In some embodiments, a fluid source may be coupled to the inflatable member and configured to inflate the inflatable member.

[0011] In some embodiments, one or more electrodes of the first set of electrodes and one or more electrodes of the second set of electrodes may have an insulated electrical lead associated therewith, the insulated electrical lead configured for sustaining a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation, the insulated electrical lead disposed in a lumen of the catheter shaft. In some embodiments, one or more electrodes of the first set of electrodes and the second electrode may have an insulated electrical lead associated therewith, the insulated electrical lead configured for sustaining a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation, the insulated electrical lead disposed in a lumen of the catheter shaft.

[0012] In some embodiments, one or more electrodes of the first set of electrodes and one or more electrodes of the second set of electrodes may be independently addressable. In some embodiments, one or more electrodes of the first set of electrodes and the second electrode may be independently addressable.

[0013] In some embodiments, a distal-most electrode of the first set of electrodes may be spaced apart from a proximal most electrode of the second set of electrodes by between about 2

mm and about 10 mm. In some embodiments, a distal-most electrode of the first set of electrodes may be spaced apart by at least about 5 mm from a proximal end of the inflatable member. In some embodiments, the first set of electrodes may be formed on a portion of the catheter shaft having a length of between about 1 mm and about 12 mm. In some embodiments, the inflatable member has a cross-sectional diameter in its equatorial plane of between about 5 mm and about 15 mm. In some embodiments, the inflatable member may have a length of up to about 22 mm. In some embodiments, each electrode of the first set of electrodes has a width of between about 1 mm and about 5 mm and wherein adjacent electrodes of the first set of electrodes are spaced apart by between about 1 mm and about 5 mm.

[0014] In some embodiments, the inflatable member may have an asymmetric shape in a proximal-to-distal direction. In some embodiments, the inflatable member may have a bulbous shape. In some embodiments, the inflatable member may have a polyhedral shape. In some embodiments, a biocompatible coating may be formed on an outer surface of the inflatable member. In some embodiments, the distal end of the catheter may extend into an inner volume of the inflatable member. In some embodiments, a set of splines may be coupled to the catheter and an inner surface of the inflatable member. The set of splines may be configured for translation along the longitudinal axis to transition between a first configuration where the set of splines are approximately parallel to the longitudinal axis and a second configuration where the set of splines bias away from the longitudinal axis.

[0015] In some embodiments, the pulse waveform may include a first level of a hierarchy of the pulse waveform in the form of a first set of pulses, each pulse having a pulse time duration, a first time interval separating successive pulses. A second level of the hierarchy of the pulse waveform includes a plurality of first sets of pulses as a second set of pulses, a second time interval separating successive first sets of pulses, the second time interval being at least three times the duration of the first time interval. A third level of the hierarchy of the pulse waveform includes a plurality of second sets of pulses as a third set of pulses, a third time interval separating successive second sets of pulses, the third time interval being at least thirty times the duration of the second level time interval. In some of these embodiments, the pulse waveform includes a fourth level of the hierarchy of the pulse waveform includes a plurality of third sets of pulses as a fourth set of pulses, a fourth time interval separating successive third sets of

pulses, the fourth time interval being at least ten times the duration of the third level time interval.

[0016] In some embodiments, a distal portion of the catheter shaft further includes a radiopaque portion. In some embodiments, the catheter shaft defines a shaft lumen therethrough. In some embodiments, the first set of electrodes are formed on a distal portion of the catheter shaft.

[0017] In some embodiments, there are no electrodes formed on the outer surface of the inflatable member. In some embodiments, a conductive element may be formed on a surface of the inflatable member. In some embodiments, the conductive element may include a set of spaced apart conductive stripes extending between ends of the inflatable member. In some embodiments, the conductive element may be electrically connected to the second set of electrodes. In some embodiments, each stripe of the set of stripes may intersect at one or more of a proximal end and a distal end of the inflatable member.

[0018] In some embodiments, the conductive element may include an interlaced structure defining a set of apertures. In some embodiments, a first conductive element may be disposed on an outer surface of the inflatable member and a second conductive element may be disposed on an inner surface of the inflatable member. The first conductive element may have an opposite polarity to the second conductive element during delivery of a pulse waveform.

[0019] In some embodiments, a first conductive element may be disposed on an outer surface of the inflatable member and a second conductive element may be disposed on an inner surface of the inflatable member. The first conductive element may have an opposite polarity to the second conductive element during delivery of the pulse waveform.

[0020] In some embodiments, the first set of electrodes may be disposed on an outer surface of the catheter shaft and one or more electrodes of the second set of electrodes may be disposed on an inner surface of the catheter shaft. In some embodiments, the second electrode may be configured to receive electrophysiology data. In some embodiments, the second electrode may be a distal electrode. In some embodiments, the second electrode may be the only electrode formed on the outer surface of the inflatable member.

[0021] In some embodiments, a distal end of the inflatable member may have a concave surface facing away from a proximal end of the inflatable member. In some embodiments, the inflatable member may have a set of curved faces. In some embodiments, at least one electrode of the second set of electrodes is formed on one face of the inflatable member. In some embodiments, one or more electrodes of the second set of electrodes may be concave.

[0022] In some embodiments, the inflatable member may have a set of curved edges. In some embodiments, each electrode of the second set of electrodes may have a diameter of between about 3 mm and about 15 mm. In some embodiments, a distal-most electrode of the first set of electrodes may be spaced apart from a proximal end of the inflatable member by at least about 3 mm. In some embodiments, the inflatable member when inflated may have a cross-sectional diameter at its largest portion of between about 6 mm and about 22 mm.

[0023] In some embodiments, the annular inflatable member when inflated may have a diameter of between about 10 mm and about 15 mm. In some embodiments, the second electrode may have a length of between about 2 mm and about 10 mm. In some embodiments, the annular inflatable member lumen may have a diameter of between about 4 mm and about 15 mm.

[0024] In some embodiments, a second set of electrodes may be formed on the inflatable member between the first set of electrodes and the second electrode. In some embodiments, the second electrode may be independently addressable. In some embodiments, each electrode of the second set of electrodes may be independently addressable.

[0025] In some embodiments, the second set of electrodes may be formed on the inflatable member on an approximate plane approximately perpendicular to the longitudinal axis. In some embodiments, each electrode of the second set of electrodes may have a circular or elliptical shape. In some embodiments, a major axis of each electrode of the second set of electrodes having the elliptical shape may be substantially parallel to the longitudinal axis.

[0026] In some embodiments, the second set of electrodes may include a distal electrode formed at a distal end of the inflatable member. In some embodiments, each electrode of the second set of electrodes may have a circular or elliptical shape. In some embodiments, a major

axis of each electrode of the second set of electrodes having the elliptical shape except the distal electrode is substantially parallel to the longitudinal axis.

[0027] In some embodiments, a method of focal ablation via irreversible electroporation includes the steps of advancing an ablation device towards an endocardial wall. The ablation device may include a catheter shaft defining a longitudinal axis and an inflatable member coupled to a distal end of the catheter shaft. The inflatable member may have an outer surface including a set of electrically conductive portions. A first set of electrodes may be formed on a surface of the catheter shaft. A second set of electrodes may be formed distal to the first set of electrodes on the surface of the catheter shaft. The second set of electrodes electrically may be coupled to the outer surface of the inflatable member and electrically isolated from the first set of electrodes. A pulse waveform may be generated. The pulse waveform may be delivered to the endocardial wall via the ablation device.

[0028] In some embodiments, one of the first set of electrodes and the second set of electrodes may be configured as anodes. The other of the first set of electrodes and the second set of electrodes may be configured as cathodes. In some embodiments, the inflatable member of the ablation device may be transitioned from a first configuration to a second configuration. In some embodiments, transitioning the inflatable member from the first configuration to the second configuration includes infusing the inflatable member with saline. In some embodiments, pulsed electric field ablation energy may be delivered through the first set of electrodes and the second set of electrodes of the ablation device. In some embodiments, the ablation device is configured to generate an electric field intensity of between about 200 V/cm and about 800 V/cm.

[0029] In some embodiments, the ablation device may include a handle. The method may further include the steps of deflecting a portion of the ablation device using the handle. In some embodiments, first electrophysiology data of the endocardial wall may be recorded. Second electrophysiology data of the endocardial wall may be recorded after delivering the pulse waveform. In some embodiments, the first electrophysiology data and the second electrophysiology data may include intracardiac ECG signal data of the endocardial wall. In some embodiments, a diagnostic catheter may be advanced into the endocardial wall and recording the first electrophysiology data and the second electrophysiology data using the

diagnostic catheter. In some embodiments, the first electrophysiology data and the second electrophysiology data may be recorded using the ablation device in the second configuration.

[0030] In some embodiments, the method may include the steps of creating a transseptal opening into a left atrium, advancing a guidewire and a sheath into the left atrium through the transseptal opening, and advancing the ablation device into a ventricle over the guidewire. In some embodiments, the method may include the steps of creating a first access site in a patient, advancing the guidewire through the first access site and into a right atrium, advancing the dilator and a sheath over the guidewire and into the right atrium, advancing the dilator from the right atrium into the left atrium through an interatrial septum to create the transseptal opening, and dilating the transseptal opening using the dilator. In some embodiments, a second access site may be created in the patient for advancing a cardiac stimulator. In some embodiments, the method may include the steps of advancing the cardiac stimulator into a right ventricle, generating a pacing signal for cardiac stimulation of the heart using the cardiac stimulator, and applying the pacing signal to the heart using the cardiac stimulator, the pulse waveform generated in synchronization with the pacing signal.

[0031] In some embodiments, the method may include the step of fluoroscopically imaging a radiopaque portion of the ablation device during one or more steps. In some embodiments, the first access site is a femoral vein. In some embodiments, the interatrial septum includes a fossa ovalis. In some embodiments, the endocardial wall is a ventricle.

[0032] In some embodiments, the pulse waveform may include a first level of a hierarchy of the pulse waveform in the form of a first set of pulses, each pulse having a pulse time duration, a first time interval separating successive pulses. A second level of the hierarchy of the pulse waveform includes a plurality of first sets of pulses as a second set of pulses, a second time interval separating successive first sets of pulses, the second time interval being at least three times the duration of the first time interval. A third level of the hierarchy of the pulse waveform includes a plurality of second sets of pulses as a third set of pulses, a third time interval separating successive second sets of pulses, the third time interval being at least thirty times the duration of the second level time interval. In some of these embodiments, the pulse waveform includes a fourth level of the hierarchy of the pulse waveform includes a plurality of third sets of

pulses as a fourth set of pulses, a fourth time interval separating successive third sets of pulses, the fourth time interval being at least ten times the duration of the third level time interval.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] FIG. 1 is a block diagram of an electroporation system, according to embodiments.

[0034] FIGS. 2A-2D are side views of an ablation device in various configurations, according to embodiments. FIG. 2A is a side view of an uninflated ablation device. FIG. 2B is a side view of an inflated ablation device. FIG. 2C is a side view of another embodiment of an inflated ablation device. FIG. 2D is a side view of another embodiment of an inflated ablation device.

[0035] FIG. 3 is a side view of an ablation device, according to other embodiments.

[0036] FIGS. 4A-4B illustrates a method for tissue ablation, according to embodiments.

[0037] FIGS. 5A-5J are side and perspective views of ablation devices, according to other embodiments. FIG. 5A is a side view of an ablation device. FIG. 5B is a cross-sectional side view of the ablation device depicted in FIG. 5A. FIG. 5C is a cross-sectional side view of another embodiment of an ablation device. FIG. 5D is a perspective view of the ablation device depicted in FIG. 5C. FIG. 5E is a cross-sectional side view of the ablation device depicted in FIG. 5C. FIG. 5F is a perspective view of another embodiment of an ablation device. FIG. 5G is a perspective view of the ablation device depicted in FIG. 5F. FIG. 5H is a perspective view of the ablation device depicted in FIG. 5F. FIG. 5I is a perspective view of another embodiment of an ablation device. FIG. 5J is a cross-sectional side view of the ablation device depicted in FIG. 5I.

[0038] FIG. 6 is an example waveform showing a sequence of voltage pulses with a pulse width defined for each pulse, according to embodiments.

[0039] FIG. 7 schematically illustrates a hierarchy of pulses showing pulse widths, intervals between pulses, and groupings of pulses, according to embodiments.

[0040] FIG. 8 provides a schematic illustration of a nested hierarchy of monophasic pulses displaying different levels of nested hierarchy, according to embodiments.

[0041] FIG. 9 is a schematic illustration of a nested hierarchy of biphasic pulses displaying different levels of nested hierarchy, according to embodiments.

[0042] FIG. 10 illustrates schematically a time sequence of electrocardiograms and cardiac pacing signals together with atrial and ventricular refractory time periods and indicating a time window for irreversible electroporation ablation, according to embodiments.

[0043] FIG. 11 is a side view of an ablation device, according to other embodiments.

[0044] FIG. 12 is a side view of an ablation device, according to other embodiments.

[0045] FIG. 13 is a side view of an ablation device, according to other embodiments.

[0046] FIG. 14 is a side view of an ablation device, according to other embodiments.

[0047] FIG. 15 is a side view of an ablation device, according to other embodiments.

DETAILED DESCRIPTION

[0048] Described here are systems, devices, and methods for ablating tissue through irreversible electroporation. Generally, a system for delivering a pulse waveform to tissue may include a signal generator configured for generating a pulse waveform and an ablation device coupled to the signal generator and configured to receive the pulse waveform. The ablation device may include a conductive inflatable member (e.g., balloon) coupled to a distal end of a catheter shaft for delivering energy to ablate tissue by irreversible electroporation. A conductive metal pattern may be disposed on an outer surface of the inflatable member. One or more electrodes may be formed proximal to the inflatable member on a surface of the catheter shaft. In some embodiments, the ablation device may be configured for delivering the pulse waveform to tissue during use via one or more of the electrodes and inflatable member that forms a bipole. In some embodiments, capacitive voltage delivery may be provided using biphasic waveforms across a thickness of the inflatable member wall. Embodiments of the ablation device described herein may deliver energy to tissue sufficient for irreversible electroporation through the inflatable member of the ablation device that functions as an electrode. The inflatable member is inflatable so as to allow an electric field and corresponding focal ablation lesions to be generated. In some embodiments, the ablation device may form focal ablation lesions at a depth

of between about 2 mm to about 15 mm or more that may be suitable to form wide and deep ablations in a ventricular wall.

[0049] In some embodiments, the ablation devices described herein may be useful in treating ventricular arrhythmias (e.g., re-entrant ventricular tachycardia) that may occur in the ventricle and cause arrhythmia due to the cardiac depolarization signal not completing a normal circuit, but rather, an alternative circuit such as looping back upon itself (e.g., re-entrant circuit). For example, the ablation devices described herein may be used for scar homogenization or “debulking” that may ablate one or more portions of scar tissue in order to electrically isolate and/or destroy re-entrant circuits. The systems, devices, and methods described herein may be used to create one or more focal ablation lesions using an endocardial approach, and in other embodiments, may be used in an epicardial approach.

[0050] In some embodiments, the ablation device may include one or more electrodes configured to receive ECG signals and used to generate an anatomical map of the patient. For example, an ECG recording electrode may be disposed on one or more of the inflatable member and catheter shaft. This may allow the ablation device to both map and ablate tissue, thereby reducing cost, complexity, and procedure time when a separate mapping catheter is not used.

[0051] The systems, devices, and methods described herein may be used to generate large electric field magnitudes at desired regions of interest to generate irreversible electroporation. An irreversible electroporation system as described herein may include a signal generator and a processor configured to apply one or more voltage pulse waveforms to a selected set of electrodes and an inflatable member of an ablation device to deliver energy to a region of interest (e.g., ablation energy for a set of tissue in a ventricle). The pulse waveforms disclosed herein may aid in therapeutic treatment of a variety of cardiac arrhythmias (e.g., atrial fibrillation, re-entry ventricular arrhythmia, ventricular tachycardia, and/or the like). In order to deliver the pulse waveforms generated by the signal generator, one or more electrodes of the ablation device may have an insulated electrical lead configured for sustaining a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation. In some embodiments, at least some of the electrodes may be independently addressable such that each electrode may be controlled (e.g., deliver energy) independently of any other electrode of

the device. In this manner, the electrodes may deliver different energy waveforms with different timing synergistically for electroporation of tissue.

[0052] The term “electroporation” as used herein refers to the application of an electric field to a cell membrane to change the permeability of the cell membrane to the extracellular environment. The term “reversible electroporation” as used herein refers to the application of an electric field to a cell membrane to temporarily change the permeability of the cell membrane to the extracellular environment. For example, a cell undergoing reversible electroporation can observe the temporary and/or intermittent formation of one or more pores in its cell membrane that close up upon removal of the electric field. The term “irreversible electroporation” as used herein refers to the application of an electric field to a cell membrane to permanently change the permeability of the cell membrane to the extracellular environment. For example, a cell undergoing irreversible electroporation can observe the formation of one or more pores in its cell membrane that persist upon removal of the electric field.

[0053] Pulse waveforms for electroporation energy delivery as disclosed herein may enhance the safety, efficiency and effectiveness of energy delivery to tissue by reducing the electric field threshold associated with irreversible electroporation, thus yielding more effective ablative lesions with a reduction in total energy delivered. In some embodiments, the voltage pulse waveforms disclosed herein may be hierarchical and have a nested structure. For example, the pulse waveform may include hierarchical groupings of pulses having associated timescales. In some embodiments, the methods, systems, and devices disclosed herein may comprise one or more of the methods, systems, and devices described in International Application Serial No. PCT/US2016/057664, filed on October 19, 2016, and titled “SYSTEMS, APPARATUSES AND METHODS FOR DELIVERY OF ABLATIVE ENERGY TO TISSUE,” the contents of which are hereby incorporated by reference in its entirety.

[0054] In some embodiments, the systems may further include a cardiac stimulator used to synchronize the generation of the pulse waveform to a paced heartbeat. The cardiac stimulator may electrically pace the heart with a cardiac stimulator and ensure pacing capture to establish periodicity and predictability of the cardiac cycle. A time window within a refractory period of the periodic cardiac cycle may be selected for voltage pulse waveform delivery. Thus, voltage pulse waveforms may be delivered in the refractory period of the cardiac cycle so as to avoid

disruption of the sinus rhythm of the heart. In some embodiments, an ablation device may include one or more catheters, guidewires, inflatable members, and electrodes. The ablation device may transform into different configurations (e.g., deflated and inflated) to position the device within an endocardial space.

[0055] Generally, to ablate tissue, one or more catheters may be advanced in a minimally invasive fashion through vasculature to a target location. The methods described here may include introducing a device into an endocardial space of the heart and disposing the device in contact with a ventricle or other cardiac surface. A pulse waveform may be generated and delivered to one or more electrodes and a conductive inflatable member of the device to ablate tissue. In some embodiments, the pulse waveform may be generated in synchronization with a pacing signal of the heart to avoid disruption of the sinus rhythm of the heart. In some embodiments, the electrodes may be configured in anode-cathode subsets. The pulse waveform may include hierarchical waveforms to aid in tissue ablation and reduce damage to healthy tissue.

I. Systems

Overview

[0056] Disclosed herein are systems and devices configured for tissue ablation via the selective and rapid application of voltage pulse waveforms to aid tissue ablation, resulting in irreversible electroporation. Generally, a system for ablating tissue described here may include a signal generator and an ablation device having one or more electrodes and an inflatable member (e.g., balloon) for the selective and rapid application of DC voltage to drive electroporation. As described herein, the systems and devices may be deployed endocardially to treat cardiac arrhythmias. Voltage pulse waveforms may be applied to a subset of the electrodes, with suitable anode/cathode electrode selections. A pacing signal for cardiac stimulation may be generated and used to generate the pulse waveform by the signal generator in synchronization with the pacing signal.

[0057] Generally, the systems and devices described herein include one or more catheters configured to ablate tissue in a ventricle of a heart. FIG. 1 illustrates an ablation system (100) configured to deliver voltage pulse waveforms. The system (100) may include an apparatus (120) including a signal generator (122), processor (124), memory (126), and cardiac stimulator

(128). The apparatus (120) may be coupled to an ablation device (110), and optionally to a pacing device (130).

[0058] The signal generator (122) may be configured to generate pulse waveforms for irreversible electroporation of tissue, such as, for example, ventricular tissue, such as that of the left ventricle. For example, the signal generator (122) may be a voltage pulse waveform generator and be configured to deliver a pulse waveform to the ablation device (110). The return electrode (140) in some embodiments may be coupled to a patient (e.g., disposed on a patient's back) to allow current to pass from the ablation device (110) through the patient and then to the return electrode (140). In other embodiments, the return electrode (140) may be part of the ablation device so that the electrode bipole is on the device. The processor (124) may incorporate data received from memory (126), cardiac stimulator (128), and pacing device (130) to determine the parameters (e.g., amplitude, width, duty cycle, etc.) of the pulse waveform to be generated by the signal generator (122). The memory (126) may further store instructions to cause the signal generator (122) to execute modules, processes and/or functions associated with the system (100), such as pulse waveform generation and/or cardiac pacing synchronization. For example, the memory (126) may be configured to store pulse waveform and/or heart pacing data for pulse waveform generation and/or cardiac pacing, respectively.

[0059] In some embodiments, the ablation device (110) may include a catheter having an inflatable member (e.g., balloon) configured to deliver the pulse waveforms described in more detail below. In each of the embodiments described herein, the inflatable member may be inflated using gas, liquid, combinations thereof, and the like. For example, the ablation device (110) may be introduced into an endocardial space and positioned to align the inflatable member to a tissue surface, and then deliver the pulse waveforms to ablate tissue. The ablation device (110) may include one or more electrodes (112), which may, in some embodiments, be independently addressable electrodes. Each electrode may include an insulated electrical lead configured to sustain a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation. In some embodiments, the insulation on each of the electrical leads may sustain an electrical potential difference of between about 200 V to about 3,000 V across its thickness without dielectric breakdown. For example, the electrodes (112) may be grouped into one or more anode-cathode subsets such as, for example, a subset including one proximal electrode and one distal electrode. In some embodiments, the distal electrode may include at

least a portion of an inflatable member. As used herein, proximal is towards a handle of an ablation device and distal is towards a tip end of the ablation device.

[0060] When used, the pacing device (130) may be suitably coupled to the patient (not shown) and configured to receive a heart pacing signal generated by the cardiac stimulator (128) of the apparatus (120) for cardiac stimulation. An indication of the pacing signal may be transmitted by the cardiac stimulator (128) to the signal generator (122). Based on the pacing signal, an indication of a voltage pulse waveform may be selected, computed, and/or otherwise identified by the processor (124) and generated by the signal generator (122). In some embodiments, the signal generator (122) may be configured to generate the pulse waveform in synchronization with the indication of the pacing signal (e.g., within a common refractory window). For example, in some embodiments, the common refractory window may start substantially immediately following a ventricular pacing signal (or after a very small delay) and last for a duration of approximately 250 ms or less thereafter. In such embodiments, an entire pulse waveform may be delivered within this duration.

[0061] The processor (124) may be any suitable processing device configured to run and/or execute a set of instructions or code. The processor may be, for example, a general purpose processor, a Field Programmable Gate Array (FPGA), an Application Specific Integrated Circuit (ASIC), a Digital Signal Processor (DSP), and/or the like. The processor may be configured to run and/or execute application processes and/or other modules, processes and/or functions associated with the system and/or a network associated therewith (not shown). The underlying device technologies may be provided in a variety of component types, e.g., metal-oxide semiconductor field-effect transistor (MOSFET) technologies like complementary metal-oxide semiconductor (CMOS), bipolar technologies like emitter-coupled logic (ECL), polymer technologies (e.g., silicon-conjugated polymer and metal-conjugated polymer-metal structures), mixed analog and digital, and/or the like.

[0062] The memory (126) may include a database (not shown) and may be, for example, a random access memory (RAM), a memory buffer, a hard drive, an erasable programmable read-only memory (EPROM), an electrically erasable read-only memory (EEPROM), a read-only memory (ROM), Flash memory, etc. The memory (126) may store instructions to cause

the processor (124) to execute modules, processes and/or functions associated with the system (100), such as pulse waveform generation and/or cardiac pacing.

[0063] The system (100) may be in communication with other devices (not shown) via, for example, one or more networks, each of which may be any type of network. A wireless network may refer to any type of digital network that is not connected by cables of any kind. However, a wireless network may connect to a wireline network in order to interface with the Internet, other carrier voice and data networks, business networks, and personal networks. A wireline network is typically carried over copper twisted pair, coaxial cable or fiber optic cables. There are many different types of wireline networks including, wide area networks (WAN), metropolitan area networks (MAN), local area networks (LAN), campus area networks (CAN), global area networks (GAN), like the Internet, and virtual private networks (VPN). Hereinafter, network refers to any combination of combined wireless, wireline, public and private data networks that are typically interconnected through the Internet, to provide a unified networking and information access solution.

Ablation Device

[0064] The systems described here may include one or more multi-electrode ablation devices configured to ablate tissue in a ventricle of a heart for treating indications such as ventricular arrhythmia. FIG. 2A is a side view of an ablation device (200) (e.g., structurally and/or functionally similar to the ablation device (110)) including a catheter shaft (210) and an inflatable member (e.g., balloon) (240) coupled to a distal end of the catheter shaft (210). In some embodiments, the ablation device (200) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle, as described herein. A distal portion of the inflatable member (240) may include and/or be formed in an atraumatic shape that reduces trauma to tissue (e.g., prevents and/or reduces the possibility of tissue puncture). The catheter shaft (210) and inflatable member (240) may be sized for advancement into an endocardial space (e.g., a left ventricle). The catheter shaft (210) may be flexible so as to be deflectable, as shown and discussed in more detail with respect to FIG. 3. Any of the catheter shafts described herein may include a shaft lumen therethrough. A set of electrical leads and/or a fluid (e.g., saline) may be disposed within the shaft lumen. The inflatable member (240) may be configured to transition between a first configuration (e.g., a deflated state) and a second

configuration (e.g., an inflated state). In the first configuration, the inflatable member (240) may have a diameter that is about the same as a diameter of the catheter shaft (210) to aid in advancing the ablation device (200) through vasculature. For example, the inflatable member (240) in the first configuration may be approximately parallel to a longitudinal axis (212) of the catheter shaft (210). For example, the inflatable member (240) may be in a compressed or crimped configuration. In the second configuration, the inflatable member (240) may have a cross-sectional diameter at its largest portion (e.g., at its equatorial plane) in the range of between approximately 5 mm and approximately 15 mm. For example, the inflatable member (240) when inflated may bias away from the longitudinal axis. The inflatable member (240), or a portion thereof, may include a conductive outer surface (e.g., FIG. 2C) that may be configured as an anode or cathode for delivery of pulse waveform to tissue.

[0065] As shown in FIGS. 2A-2D, one or more electrodes (220, 230) may include a series of metallic bands or rings disposed along a surface of a catheter shaft (210). For example, the ablation device (200) may comprise a first set of electrodes (220) (e.g., one or more proximal electrodes) formed on a surface of a distal portion of the catheter shaft (210). In some embodiments, one or more electrodes (220, 230) may be formed on the catheter shaft (210) along its entire circumference. In some embodiments, one or more electrodes (220, 230) may be formed on the surface of a portion of a circumference of the catheter shaft (210). For example, electrode (220) may encircle the circumference of the catheter shaft (210). In some embodiments, one or more electrodes may be fully covered by a thin layer of dielectric coating for biphasic operation.

[0066] In FIGS. 2A-2B, there are no electrodes formed on the outer surface of the inflatable member (240). In some embodiments, the ablation device (200) may comprise a second set of electrodes (230) (e.g., a single distal electrode). The second set of electrodes (230) may be formed distal to the first set of electrodes (210) on the surface of the distal portion of the catheter shaft (210). In some embodiments, the electrodes (220, 230) may be shaped to conform to the shape of the catheter shaft (210). For example, the electrodes may be press fit (e.g., crimped) to the catheter shaft (210) or attached using a conductive adhesive. The catheter shaft (210) may include flexible portions (e.g., may be deflectable) between the electrodes (220, 230) to enhance flexibility and allow the device (200) to be deflected and aid in advancement through

vasculature. In other embodiments, one or more electrodes (220, 230) may include a helical winding to enhance flexibility.

[0067] Each of the electrodes of any of the ablation devices discussed herein may be connected to an insulated electrical lead (not shown) leading to a handle (not shown) coupled to a proximal portion of the catheter. The insulation on each of the electrical leads may sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown. In other embodiments, the insulation on each of the electrical leads may sustain an electrical potential difference of between about 200 V to about 3,000 V across its thickness without dielectric breakdown, including all values and sub-ranges in between. This allows the electrodes and inflatable member coupled thereto to effectively deliver electrical energy and to ablate tissue through irreversible electroporation. The electrodes (220, 230) may, for example, receive pulse waveforms generated by a signal generator (122) as discussed above with respect to FIG. 1.

[0068] The first set of electrodes (220) may be electrically coupled together using one or more electrical leads. The second set of electrodes (230) may be electrically coupled together using a different set of electrical leads. An outer surface of the inflatable member (240) may include a set of electrically conductive portions and coupled to the second set of electrodes (230) and electrically isolated from the first set of electrodes (220). In some embodiments, the first set of electrodes (220) may be configured as an anode while the second set of electrodes (230) and inflatable member (240) may be configured as a cathode. Accordingly, a bipole may be formed between the first set of electrodes (220) and the inflatable member (240) that results in an electric field capable of ablating tissue (e.g., myocardial cells on an inner surface or within a ventricle). The inflatable member (240) and the first set of electrodes (220) may be electrically isolated from each other. For example, the second set of electrodes (230) and the first set of electrodes (220) may each couple to a respective insulated electrical lead, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown. In some embodiments, the first set of electrodes (220) may have an opposite polarity to the second set of electrodes (230) during delivery of a voltage pulse waveform.

[0069] The first and second sets of electrodes (220, 230) may include an atraumatic shape to reduce trauma to tissue. For example, the electrodes (220, 230) may have an atraumatic shape

including a rounded, flat, curved, and/or blunted portion. For example, the electrodes (220, 230) in FIGS. 2A-2D may be ring electrodes. In some embodiments, the first set of electrodes (220) may be located along any portion of the catheter shaft (210) proximal to the second set of electrodes (230). The second set of electrodes (230) may be disposed on a surface of the catheter shaft (240) and/or flush with the surface of the inflatable member (240) so as to be electrically coupled to the inflatable member (240). The electrodes (220, 230) may have the same or different sizes, shapes, and/or location along the catheter shaft (210). The spacing between electrodes of the first set of electrodes (220) may be configured to allow a distal portion of the catheter shaft (210) (e.g., deflectable portion) to deflect a predetermined amount (e.g., up to about 210 degrees of deflection). For example, the deflectable portion may be configured for deflecting a portion of the catheter including the second set of electrodes (230) and the inflatable member (240) up to about 210 degrees relative to the longitudinal axis.

[0070] In some embodiments, the first set of electrodes (220) may include electrodes disposed along a portion of the catheter shaft (210) having a length between about 1 mm and about 12 mm from a proximal end to a distal end of the first set of electrodes (220). The first set of electrodes (220) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode) while allowing the catheter shaft (210) to remain flexible and facilitate deflection. In some embodiments, the first set of electrodes (220) may be spaced apart from the second set of electrodes (230) by a length of between about 2 mm and about 10 mm.

[0071] For each of the ablation devices discussed herein, the electrodes (220, 230) may include biocompatible metals such as titanium, palladium, gold, silver, platinum or a platinum alloy. For example, the electrode may preferably include platinum or a platinum alloy. In some embodiments, the proximal electrodes may have a biocompatible coating that permits capacitive voltage delivery with biphasic waveforms. Each electrode (220, 230) may include an electrical lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown. In other embodiments, the insulation on each of the electrical leads may sustain an electrical potential difference of between about 200 V to about 3,000 V across its thickness without dielectric breakdown, including all values and sub-ranges in between. The insulated electrical leads may run to the proximal handle portion of the ablation device (200) from where they may be connected to a suitable electrical connector. The

catheter shaft (210) may be made of a flexible polymeric material such as Teflon, Nylon, Pebax, etc.

[0072] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (220, 230) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. Electrophysiology data may be used to generate an anatomical map that may be used to compare electrophysiology data recorded after energy delivery. The electrophysiology data may include intracardiac ECG signal data. The ablation device (200) may include one or more ECG signal electrodes. For example, one or more electrodes of the first set of electrodes (220) may be configured to receive an ECG signal. In some embodiments, an ECG signal electrode may be disposed on a surface of a distal end of an inflatable member (240) (not shown). The ECG signal electrode may be coupled to its own insulated electrical lead. The ECG signal electrode may be electrically isolated from the inflatable member (240) using, for example, a ring of insulation around the ECG signal electrode electrically isolating the ECG signal electrode from the conductive inflatable member. In these embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation. In some embodiments, the ablation device (200) may include a location sensor that may generate location data of the ablation device disposed within vasculature. The electrophysiology data and location data may be used to generate an anatomical map of the electrophysiology data. In some embodiments, the location sensor may include an electromagnetic coil disposed at a distal end of the inflatable member (240). In other embodiments, the location sensor may be disposed within a lumen of the catheter shaft (210).

[0073] In some embodiments, the inflatable member (240) may be coupled to the second set of electrodes (230), and configured to deliver a pulse waveform from a signal generator to tissue during use. The inflatable member (240) may be coupled to a distal portion of the catheter shaft (210) and configured to be conductive so as to function as one half of an anode-cathode pair for delivery of irreversible electroporation energy to tissue. The inflatable member (240) may be configured to transition between a first configuration (e.g., deflated inflatable member in FIG. 2A) and a second configuration (e.g., inflated inflatable member in FIGS. 2B-2D). The inflatable member (240) in the first configuration may be in a compact, deflated state suitable for advancement through vasculature. For example, the inflatable member (240) in the first configuration may be substantially empty of fluid, such as saline. The inflatable member (240) in

the second configuration may hold a predetermined volume of saline that fills and inflates the inflatable member (240) to a predetermined size and shape (e.g., having a diameter to contact a diameter of a ventricle). The inflatable member (240) may transition to an intermediate configuration between the first and second configuration as necessary, for example, to conform to a lumen or advance the device through vasculature.

[0074] In some embodiments, the inflatable members as described herein may have an expandable structure and may be composed of materials including, but not limited to polyvinyl chloride (PVC), polyethylene (PE), cross-linked polyethylene, polyolefins, polyolefin copolymer (POC), polyethylene terephthalate (PET), nylon, polymer blends, polyester, polyimide, polyamides, polyurethane, silicone, polydimethylsiloxane (PDMS), and the like. The inflatable member may be embedded with other materials including, but not limited to metals, insulation, Kevlar, nylon fibers, and the like.

[0075] The distal portion of the inflatable member (240) disposed in a lumen (e.g., ventricle) may serve as a backstop to advancement of a distal portion of the catheter (200). By modifying a size of the inflatable member (240) and manipulating the deflection of the catheter shaft (210), the inflatable member (240) may be positioned at a target tissue site, such as, for example, near or in contact with the wall of a left ventricle. The distal portion of the catheter shaft (210) may include a set of electrodes (220, 230) (e.g., structurally and/or functionally similar to the electrode(s) (112)) where the inflatable member (240) may be configured to contact an inner radial surface of a tissue lumen (e.g., ventricle). In some embodiments, a cross-sectional diameter of the inflatable member (240) at its largest portion (e.g., equatorial plane) when inflated may be between about 5 mm and about 15 mm. A length of the inflatable member (240) when inflated may be up to about 22 mm. In some embodiments, the length of the inflatable member (240) may be substantially the same between the first and second configurations.

[0076] A proximal end of the inflatable member (240) may be coupled to a suitable electrical lead (e.g., via a second set of electrodes (230)) and connected to the signal generator (122) of FIG. 1. The inflatable member (240) may be configured as a cathode and the first set of electrodes (220) may be configured as an anode, or vice versa. In some embodiments, as described in detail herein, a set of proximal electrodes (220) and the inflatable member (240) may form a bipole. In this manner, the inflatable member (240) in the second configuration may

be placed against, for example, an inner wall of the left ventricle in order to directly generate localized or focal lesions thereupon by activation of the first and second set of electrodes (220, 230) using any suitable combination of polarities. For example, the first and second set of electrodes (230, 240) may be configured with opposite polarities. In some embodiments, the ablation device may be configured to generate an electric field having an intensity of at least about 200 V/cm.

[0077] One or more of a biphasic signal may be applied to the bipole such that tissue may be ablated between the inflatable member (240) and the first set of electrodes (220) at a desired location in the ventricle. For example, a biphasic pulse waveform may be delivered between the sets of electrodes of opposed polarities, resulting in a zone of irreversible electroporation ablation in the region around the inflatable member.

[0078] In some embodiments, the inflatable member (240) when inflated may be configured to contact endocardial tissue while the second set of electrodes (220) (also sometimes referred to as “proximal electrodes”) in the second configuration may not contact endocardial tissue. The electric field generated by the ablation device (200) due to conduction between the inflatable member (240) and proximal electrodes (220) through the blood pool and through tissue may result in focal ablation of tissue via irreversible electroporation.

[0079] In general, the inflatable member (240) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (240) is more bulbous than the other end (for example the proximal end) of the inflatable member (240). The inflatable member (240) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (210). Such a bulbous distal portion can aid in positioning the device (200) in a ventricle as well as further controlling a size and depth of focal ablation. In this manner, the inflatable member (240) when inflated may be placed against, for example, an endocardial surface such as the inner surface of a ventricle in order to directly generate lesions thereupon by activation of appropriate electrodes (220, 230) using any suitable combination of polarities. For example, the inflatable member (240) may be placed at an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion).

[0080] In some embodiments, an outer surface of the inflatable member (240) may include a set of conductive (e.g., metallized) portions. In this configuration, a bipole may be formed between the outer surface of the inflatable member (240) and the first set of electrodes (220) (e.g., proximal electrodes). For example, the outer surface of the inflatable member (240) may include a deposition of a biocompatible metal material (e.g., gold, silver, platinum), metal plating, printed metal nanoparticle ink, and/or the like. A portion of the inflatable member may include metal foil. The density of the metal material disposed on the outer surface of the inflatable member (240) may be such as to ensure electrical coupling with the second set of electrodes (230) (e.g., a distal ring electrode). The second set of electrodes (230) may be electrically coupled to a set of electrically conductive portions of the outer surface of the inflatable member (240) such that the inflatable member (240) is electrically coupled to a respective electrical lead. The electrode leads may be configured with sufficient insulation and high dielectric strength to be suitable for delivery of irreversible electroporation energy as described herein.

[0081] As shown in FIG. 2C, an ablation device (200') may include a catheter shaft (210') coupled at a distal end to an inflatable member (e.g., balloon) (240'). A first set of electrodes (220') and a second set of electrodes (230') may be disposed on a surface of the catheter shaft (210') and/or flush with the surface. In some embodiments, one or more portions of the inflatable member (240') may be conductive. For example, the entire outer surface of the inflatable member (240') may be conductive or predetermined portions of the inflatable member (240') may be conductive and coupled to the second set of electrodes (230'). As shown in FIG. 2C, the outer surface of the inflatable member may include one more conductive elements (e.g., pattern) (242') having a set of spaced apart conductive stripes extending in a proximal-to-distal direction between the ends of the inflatable member (240'). The one or more conductive elements (242') may be electrically isolated from each other. The conductive stripes may be formed by techniques such as masked electrodeposition. In some embodiments, the conductive element (242') may be disposed symmetrically on the inflatable member (240'). Each of the stripes of the conductive element (242') may be electrically coupled to the distal electrode (230'). The stripes may intersect each other at proximal and distal ends of the inflatable member (240') and/or between the ends of the inflatable member (240'). The inflatable member (240') may be flexible and/or expandable between the metal stripes of the conductive element (242'). The conductive

element (242') may be disposed (e.g., deposited) on the inflatable member (240') in a manner that maintains electrical coupling with an electrical lead in the first configuration, second configuration, and configurations in-between. The conductive element (242') may provide rigidity and/or stiffness to the inflatable member (240') and aid in advancement of the inflatable member (240') through vasculature. In some embodiments, the conductive element (242') may include one or more spiral shaped metal portions. In some embodiments, the conductive element (242') may include an interlaced structure (e.g., mesh shape). For example, the interlaced structure may form a set of polygonal apertures (e.g., openings) including one or more of a circular shape, parallelogram, hexagonal, and the like.

[0082] As shown in FIG. 2D, an ablation device (200'') may include a catheter shaft (210'') coupled at a distal end to an inflatable member (e.g., balloon) (240''). A first set of electrodes (220'') may be disposed on an outer surface of the catheter shaft (210''). A second set of electrodes (235'') may be disposed on an inner surface of the catheter shaft (210''). In some embodiments, one or more portions of the inflatable member (240'') may include a metal electrode portion (245'') (e.g., second electrode). In some embodiments, the second electrode (245'') is the only electrode formed on the outer surface of the inflatable member. A portion (245'') of the inflatable member surface (240'') may be metal. For example, a portion (245'') of the inflatable member (240'') may be a distal portion. In some embodiments, the inflatable member (240'') may define an inflatable member lumen (237'') extending along a first longitudinal axis of the catheter shaft (210'') to a distal end of the inflatable member (240''). A proximal end of an electrical lead (239'') may couple to the distal electrode (235'') and extend through the inflatable member lumen (237'') to couple to the electrode portion (245'') at a distal end of the inflatable member (240''). Accordingly, the electrode portion (245'') may be configured to deliver irreversible electroporation voltage pulses. In some embodiments, the portion (245'') (e.g., formed of metal) of the inflatable member (240'') may be configured as an electrode of one polarity while the first set of electrodes (220'') (e.g., proximal electrode(s)) may be configured as electrode(s) of the opposite polarity.

[0083] In some embodiments, a metallized outer surface of the inflatable member as discussed herein may be further covered by a layer of biocompatible material. The biocompatible coating may help prevent fibrin deposition due to high voltage energy delivery to tissue by the ablation device. In this configuration, a bipole may be formed between the outer surface of the inflatable

member and the first set of electrodes (e.g., proximal electrode). However, the ablation device may be configured to deliver energy using one or more biphasic waveforms capacitively across the biocompatible coating on the inflatable member.

[0084] In some embodiments, the ablation device (200) may not include a second set of electrodes (230) (e.g., distal electrode) disposed on an outer surface of the catheter shaft (210). Instead, the inflatable member (240) may be configured to include an inner and outer metallized surface that sandwiches the inflatable member (240). The inner and outer metallized surface may include any combination of conductive elements (242) described herein. An electrical lead may be directly connected to the inner metallized surface of the inflatable member (240). In this configuration, a bipole may be formed between the inflatable member (240) and the first set of electrodes (220).

[0085] Activation of the first and second sets of electrodes using a predetermined configuration of the inflatable member may provide targeted and precise focal ablation by controlling a focal ablation spot size based on the expansion of the inflatable member. As described herein, focal ablation of tissue may be used to treat ventricular arrhythmia. For example, when the inflatable member of the ablation device is partially filled with saline, a high intensity electric field having a relatively smaller/more focused diameter results in a focal ablation lesion that is relatively smaller in diameter and shallower in depth. When the inflatable member of the ablation device is in the second configuration (e.g., full inflation state), a relatively larger and more dispersed electric field is generated, resulting in a focal ablation lesion that is relatively wider and deeper. In this manner, by varying the extent of expansion of the inflatable member, the depth and/or size of the lesion may be controlled with a single ablation device. Such aspects are useful for creating multiple lesions of varying sizes and/or depths using the same ablation device. Saline may be used to inflate the inflatable member and is not used for conduction. If the inflatable member (which is non-porous) is punctured or otherwise breaks, the saline may safely leak out of the inflatable member.

[0086] In some embodiments, a distal end of the catheter shaft (210) may extend into an internal cavity of the inflatable member (240) to provide rigidity and support to a distal end of the ablation device (200) that may aid in advancement of the ablation device (200) through vasculature. The added rigidity may further provide additional tactile feedback to an operator.

For example, a distal end of the catheter shaft (210) coupled to a distal end of the inflatable member (240) may provide sufficient support and rigidity in advancing the inflatable member (240) through a transseptal puncture. In some embodiments, the distal end of the catheter shaft (210) may include a set of splines within the inflatable member that bias away from a longitudinal axis of the catheter shaft (210) and connect together at a distal end of the inflatable member (240). For example, the set of splines may be coupled to the catheter shaft (210) and an inner surface of the inflatable member (240) and configured for translation along the longitudinal axis to transition between a first configuration where the set of splines are approximately parallel to the longitudinal axis and a second configuration where the set of splines bias away from the longitudinal axis. The set of splines may form a basket-like shape to provide rigidity and support to the inflatable member. In some embodiments, the distal end of the catheter shaft (210) may be configured with a predetermined stiffness different from the stiffness of the catheter shaft (210) proximal to the inflatable member (240). For example, the distal end of the catheter shaft (210) within the inflatable member (240) may be stiffer than deflectable portions of the catheter shaft (210).

[0087] In some embodiments, one or more distal portions of the catheter shaft (210) may include a radiopaque portion. For example, the distal portion of the catheter shaft (210) may include a radiopaque platinum coil within a cavity of the inflatable member (240). The radiopaque portion may be fluoroscopically imaged to aid an operator in locating and positioning the ablation device (200) within one or more body cavities of the patient. The radiopaque portion may include a set of marker bands. In some embodiments, one or more splines of the distal portion (e.g., distal end) of the catheter shaft (210) may include a radiopaque portion (not shown) formed on a surface of that spline. Additionally or alternatively, a location sensor may be coupled to the distal end of the catheter shaft (210) within the inflatable member (240).

[0088] FIG. 3 is a side view of another embodiment of an ablation device (300) (e.g., structurally and/or functionally similar to the ablation device (110, 200)) including a catheter shaft (310) having a first set of electrodes (320) provided proximal to a second set of electrodes (330) and an inflatable member (e.g., balloon) (340). The first set of electrodes may be formed on a surface of a distal portion of the catheter shaft (310). During use, the electrodes (320, 330)

may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue (350), as described in more detail herein.

[0089] In some embodiments, a handle (not shown) may be coupled to a proximal portion of the ablation device (300) and may include a bending mechanism (e.g., one or more pull wires (not shown)) configured to modify the shape of the distal portion of the catheter shaft (310). For example, operation of a pull wire of the handle may increase or decrease a curvature in a deflectable portion (312) (e.g., bend in the catheter shaft (310)) in the distal portion of the catheter shaft (310). In some embodiments, the catheter (300) may have a deflectable portion (312) proximal to the second set of electrodes (330) and/or the first set of electrodes (320). The deflectable portion may be configured to deflect up to about 210 degrees relative to the longitudinal axis of the catheter shaft (310). The curvature in the deflectable portion (312) of the catheter shaft (310) may be modified to allow the electrodes (320, 330) and inflatable member (340) to be disposed near and/or in contact with a tissue surface (350) (e.g., in contact with an inner radial surface of a ventricle). In this manner, apposition of the ablation device (300) to tissue may be provided at a desired position and orientation (e.g., the inflatable member may be perpendicular, angled, or parallel to the tissue surface).

[0090] In some embodiments, the pulse waveform may be applied between the first set of electrodes (320) and the inflatable member (340) configured in anode and cathode sets. It should be appreciated that any of the pulse waveforms disclosed herein may be progressively or sequentially applied to the set of anode-cathode pairs. In some embodiments, the first set of electrodes (320) may have an opposite polarity to the second set of electrodes (330) during delivery of a voltage pulse waveform. The electrodes (320, 330) may include a series of metallic bands or rings and in some embodiments may be independently addressable. In some embodiments, the electrical leads of at least two electrodes of the first set of electrodes (320) may be electrically coupled at or near a proximal portion of the ablation device, such as, for example, within the handle.

[0091] FIG. 5A is a side view of an ablation device (500) (e.g., structurally and/or functionally similar to the ablation device (110)) including a catheter shaft (510) and an inflatable member (e.g., balloon) (540) coupled to a distal end of the catheter shaft (510). In some embodiments, the ablation device (500) is useful for forming lesions on endocardial surfaces (555) via focal

ablation. FIG. 5B illustrates spatial zones (530, 532) that may correspond to tissue ablation zones of sufficiently high electric field intensities to generate focal ablation lesions on a tissue surface (555). As shown in FIG. 5A, the inflatable member (540) may generally have a portion (545) that may be configured as a second electrode and which may be at least partly metallic. In some embodiments, the first set of electrodes (520) of the ablation device (500) may be configured as cathodes and the second electrode (545) may be configured as an anode, or vice versa. In some embodiments, the first set of electrodes (520) may have an opposite polarity to the second electrode (545) during delivery of a voltage pulse waveform. The first set of electrodes (520) may be formed on a surface of a distal portion of the catheter shaft (510). The flat distal second electrode (545) of the inflatable member (540) may be disposed against a tissue surface, such as a ventricular wall (555). The inflatable member (540) in the second configuration may have a circular cross-section. For example, the inflatable member (545) may have a diameter of about 12 mm and a voltage potential difference of about 2,000 V may be applied between the anode (520) and cathode (545) electrodes. In some embodiments, the first set of electrodes (520) may have a width of about 3 mm each and a separation of about 3 mm between adjacent electrodes. In some embodiments, the most distal electrode of the first set of electrodes (520) may be separated from the inflatable member (540) by at least about 5 mm.

[0092] FIG. 5B illustrates first and second spatial zones (530, 532) corresponding to an electric field intensity of magnitude of at least about 460 V/cm when a potential difference of about 2,000 V is applied between the anode (520) and cathode (545) electrodes with the distal flat electrode (545) disposed against the tissue wall (555). The second spatial zone (532) overlapping the tissue wall (555) may have a depth of about 7 mm and a width of about 20 mm.

[0093] In some embodiments, an ablation device (500') may include an inflatable member (540') having a distal portion having a concave surface facing away from a proximal end of the inflatable member (540'). As shown in FIGS. 5C and 5D, an inflatable member (540') may include a first curved portion (544') and a second curved portion (545'). The first curved portion (544') may include a portion of the inflatable member (540') configured to be in contact with an endocardial surface (555') as shown in FIG. 5E.

[0094] In some embodiments, for example as shown in FIG. 5C, the inflatable member (540') may include an inflatable member lumen (537') extending along a first longitudinal axis of the

catheter shaft (510') from a distal end of the catheter shaft (510') to a distal end of the inflatable member (540'). A proximal end of an electrical lead (539') may couple to a second set of electrodes (535') (e.g., distal electrode) and extend through the inflatable member lumen (537') to couple to the electrode portion (545') at a distal end of the inflatable member (540').

Accordingly, the electrode portion (545') may be configured to deliver irreversible electroporation voltage pulses. The first set of electrodes (520') and the portion (545') may be configured with opposite polarities.

[0095] FIG. 5D is a perspective view of the inflatable member (540') of FIG. 5C having a metallic concave portion (545') covering substantially an entire distal surface of the inflatable member (540'). For example, the inflatable member (545') may have a diameter of about 12 mm and, for example, a voltage potential difference of about 2,000 V may be applied between the inflatable member (545') (e.g., anode) and the first set of electrodes (520') (e.g., cathodes). In some embodiments, the first set of electrodes (520') may have a width of about 3 mm and a separation of about 3 mm between them. The distal-most electrode of the first set of electrodes (520') may be separated from the inflatable member (540') by about 5 mm. The first set of electrodes (520') have a width of about 3 mm and a separation of about 3 mm between them. The most distal electrode of the first set of electrodes (520') may have a separation of about 7 mm from the inflatable member (540'). These dimensions are provided as examples for illustrative purposes only and other values may be chosen for these as found convenient for the clinical application.

[0096] FIG. 5E illustrates first and second spatial zones (530', 532') corresponding to an electric field intensity sufficient to generate focal ablation lesions. The second ablation zone (532') may correspond to a tissue ablation zone when the inflatable member (540') is disposed against the tissue wall (555'). In some embodiments, the second set of electrodes (535') and portion (545') (e.g., comprising metal) of the inflatable member (540') may be configured as an electrode of one polarity while the first set of electrodes (520') (e.g., proximal electrode(s)) may be configured as electrode(s) of the opposite polarity. FIG. 5E illustrates first and second spatial zones (530', 532') corresponding to an electric field intensity having a magnitude of at least about 460 V/cm when a potential difference of about 2,000 V is applied between the anode (520') and cathode (545') electrodes with the distal curved electrode portion (545') (e.g., concave) disposed against the tissue wall (555'). The second spatial zone (532') overlapping the

tissue wall (555') may have a depth of about 5 mm and a width of about 21 mm. In some variations, the second spatial zone (532') may have a depth of up to about 10 mm and a width of up to about 30 mm.

[0097] FIGS. 5F and 5G illustrate an ablation device (500'') (e.g., structurally and/or functionally similar to the ablation device (110)) including a catheter shaft (510'') and an inflatable member (540'') coupled to a distal end of the catheter shaft (510''). In some embodiments, the ablation device (500'') is useful for forming lesions on endocardial surfaces via focal ablations. In some embodiments, the inflatable member (540'') may have a multi-faceted shape. In some embodiments, the multi-faceted shape may generally be a polyhedral shape with one or more second electrodes (504'') disposed on portions of one or more faces (511'') of the polyhedron. A first set of electrodes (520'') may be disposed on the catheter shaft (510''). The inflatable member (540'') may generally have one or more second electrode portions (504'') that may be configured as an electrode of the second set of electrodes and which may include metal. The inflatable member (540'') in the second configuration may have a polyhedron shape with one or more faces (511''). The second electrode portions (504'') may be electrically wired together to function as a single electrode or wired separately as independent electrodes. FIG. 5F illustrates a dodecahedron-shaped inflatable member (540'') having second electrode portions (504'') on six of the faces (511''). In some embodiments, the first set of electrodes (520'') may have an opposite polarity to the second electrode portions (504'') during delivery of a voltage pulse waveform. In some embodiments, one or more faces (511'') of the polyhedron may have a curved face.

[0098] In some embodiments, one or more of the second electrode portions (504'') of the second set of electrodes may be configured to receive ECG signals, as described herein. The strength and/or pattern of the ECG signal received by the one or more second electrode portions (504'') may be used to determine a level of contact each of the second electrode portions (504'') has with tissue (e.g., cardiac chamber wall). A set of the second electrode portions (504'') may be selected using the ECG signals to be configured as an anode or cathode. Thus, one or more second electrode portions (504'') disposed on corresponding faces (511'') of the inflatable member (540'') may be used for tissue ablation based on an ECG signal strength corresponding to tissue contact. In some embodiments, the edges of the faces (511'') (e.g., polyhedral surfaces) may be rounded so as to form a "soft" face.

[0099] In some embodiments, one or more of the second set of electrodes (504'') disposed on a face (511'') may include a concave curved shape (e.g., the electrodes may be indented) such that those faces (511'') may form a pocket configured to contact a tissue surface. The edges (515'') of these faces (511'') may have a higher stiffness than the faces (511'') themselves such that the inflatable member (540'') in the second configuration may form a polyhedron shape having one or more indented faces (511'').

[0100] FIG. 5G is another perspective view of the ablation device (500'') having an inflatable member (540'') having a generally polyhedron shape with metallized electrodes (504'') disposed on a portion of one or more faces (511'', 512'', 513'', 514'') of the inflatable member (540''). In some embodiments, a catheter shaft (510'') may define a catheter shaft lumen (not shown) configured for saline infusion to inflate the inflatable member (540''). Electrical leads may also be disposed within the catheter shaft lumen and configured to connect to the one or more electrodes (504''). Edges (515'') of the faces (511'', 512'', 513'', 514'') may be rounded and have a higher stiffness than a surface of the face so as to form an indented face surface when in the second configuration. In some embodiments, the diameter of the inflatable member (540'') in the second configuration may be between about 6 mm and about 22 mm. The first set of electrodes (520'') may be separated by at least about 3 mm or more from a proximal end of the inflatable member (540''). The metallized electrode portions (504'') may have a diameter between about 6 mm and about 15 mm. In some embodiments, the edges (522''') of one or more faces (511''') of the inflatable member (540''') may be curved. As shown in FIG. 5H, one or more electrode portions (504''') of the second set of electrodes may be disposed on a face (511''') of the inflatable member (540'''). The curved edges (522''') (e.g., polyhedral surface) may form a soft face (511''').

[0101] FIG. 5I illustrates an ablation device (500''') (e.g., structurally and/or functionally similar to the ablation device (110)) including a catheter shaft (510''') and an inflatable member (e.g., balloon) (540''') coupled to a distal end of the catheter shaft (510'''). In some embodiments, the ablation device (500''') is useful for forming lesions on endocardial surfaces via focal ablation. In some embodiments, the inflatable member (540''') may define an annular inflatable member lumen (533''') (e.g., having an annular shape) and include a distal face (545''') with a first electrode portion. The distal face (545''') may have a substantially planar portion. A second electrode (535''') (e.g., needle) may be disposed within the inflatable member

lumen (533''') and may extend out from, and distal to, the inflatable member lumen (533''') along a longitudinal axis of the inflatable member (540'''). The inflatable member (540''') may have a flat distal face (545''') that may be metallized and configured as the first electrode. The annular space defined by the inflatable member lumen (533''') may separate the second electrode (535''') from the annular inflatable member (540''') to prevent flash arcing when the second electrode (535''') and the first electrode portion (545''') are polarized with opposite electrical polarities. For example, the needle may have a length between about 8 mm and about 10 mm. The inflatable member (540''') may have a diameter of about 12 mm. The inflatable member lumen (533''') may have a diameter between about 4 mm and about 8 mm.

[0102] FIG. 5J illustrates a spatial zone (532''') corresponding to an electric field intensity of magnitude of at least about 460 V/cm when a potential difference of about 2,000 V is applied between the electrode (535''') and electrode portions (545''') with the flat distal electrode (545''') disposed against the tissue wall (555'''). The spatial zone (532''') overlapping the tissue wall (555''') may have a depth of about 10 mm and a width of about 14 mm.

[0103] FIG. 11 is a side view of another embodiment of an ablation device (1100) (e.g., structurally and/or functionally similar to the ablation device (110, 200, 300, 500, 500', 500'', 500''')) including a catheter shaft (1110) having a first set of electrodes (1120) provided proximal to a second set of electrodes (1130, 1132) and an inflatable member (e.g., balloon) (1140). The first set of electrodes (1120) may be formed on a surface of a distal portion of the catheter shaft (1110). That is, the first set of electrodes (1120) may be formed on a surface of the distal end of the catheter shaft (1110). The second set of electrodes (1130, 1132) may be formed on a surface of a distal end of the inflatable member (1140) and may be electrically isolated from the first set of electrodes (1120). In some embodiments, a major axis (e.g., longitudinal axis) of the second electrodes (1132) may be substantially parallel to the longitudinal axis of the catheter shaft (1110) and/or inflatable member (1140).

[0104] In some embodiments, the ablation device (1100) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle. During use, the electrodes (1120, 1130, 1132) may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue, as described in more detail herein. A distal portion of the inflatable member (1140) may include and/or be formed in an atraumatic shape that reduces trauma to

tissue (e.g., prevents and/or reduces the possibility of tissue puncture). The catheter shaft (1110) and inflatable member (1140) may be sized for advancement into an endocardial space (e.g., left ventricle). The catheter shaft (1110) may be flexible so as to be deflectable. For example, a deflectable portion of the catheter shaft (1110) may be configured for deflecting a portion of the catheter (1100) including the second set of electrodes (1130, 1132) and the inflatable member (1140) up to about 210 degrees relative to the longitudinal axis. The inflatable member (1140) may be configured to transition between a first configuration (e.g., deflated state) and a second configuration (e.g., inflated state). In the first configuration, the inflatable member (1140) may have a diameter that is about the same as a diameter of the catheter shaft (1110) to aid in advancing the ablation device (1100) through vasculature. For example, the inflatable member (1140) in the first configuration may be approximately parallel to a longitudinal axis of the catheter shaft (1110). The inflatable member (1140) in the second configuration may bias away from the longitudinal axis. The first set of electrodes (1120) may be structurally and/or functionally similar to the electrodes (220, 230) described with respect to FIGS. 2A-2D.

[0105] The first set of electrodes (1120) may be electrically coupled together using one or more electrical leads. The second set of electrodes (1130, 1132) may be electrically coupled together using a different set of electrical leads. In some embodiments, the inflatable member (1140) may be electrically coupled to the second set of electrodes (1130, 1132). A voltage pulse waveform delivered between the first set of electrodes (1120) and the inflatable member (1140) electrically coupled to the second set of electrodes (1130, 1132) may be used to form a lesion via focal ablation (e.g., a spot lesion) of a predetermined size and shape. In some embodiments, the first set of electrodes (1120) may be configured as an anode while the second set of electrodes (1130, 1132) and inflatable member (240) may be configured as a cathode, or vice versa. Accordingly, a bipole may be formed between the first set of electrodes (1120) and the inflatable member (1140) that results in an electric field capable of ablating tissue (e.g., myocardial cells on an inner surface or within a ventricle). The inflatable member (1140) and the first set of electrodes (1120) may be electrically isolated from each other. For example, the second set of electrodes (1130, 1132) and the first set of electrodes (1120) may each couple to a respective insulated electrical lead, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown.

[0106] The first and second sets of electrodes (1120, 1130, 1132) may include an atraumatic shape to reduce trauma to tissue. For example, the first set of electrodes (1120) may be ring electrodes. In some embodiments, the first set of electrodes (1120) may be located along any portion of the catheter shaft (1110) proximal to the second set of electrodes (1130, 1132). The first set of electrodes (1120) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode) while allowing the catheter shaft (1110) to remain flexible and facilitate deflection. The second set of electrodes (1130, 1132) may be disposed on a surface of the inflatable member (1140) and/or flush with the surface of the inflatable member (1140) so as to be electrically coupled to the inflatable member (1140). The second set of electrodes (1130, 1132) may have the same or different sizes, shapes, and/or location along the inflatable member (1140).

[0107] For example, the second set of electrodes (1130, 1132) may include a distal tip electrode (1130) and a set of generally circular or elliptically-shaped electrodes (1132) disposed around a circumference of the inflatable member (1140). For example, the second set of electrodes (1130) may be formed on the inflatable member (1140) on an approximate plane approximately perpendicular to the longitudinal axis. In some embodiments, each electrode of the second set of electrodes (1130, 1132) may be wired together. In other embodiments, subsets of the electrodes of the second set of electrodes (1130, 1132) may be electrically wired together while other subsets may be independently addressable. In some embodiments, the distal tip electrode (1132) may be electrically isolated from the first set of electrodes (1120). In some embodiments, each electrode of the second set of electrodes (1130, 1132) may be independently addressable. The distal tip electrode (1132) may be formed at a distal portion of the inflatable member (1140) and electrically isolated from the first set of electrodes (1120). The distal tip electrode (1132) may have a diameter in the range between about 3 mm and about 10 mm.

[0108] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (1120, 1132) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. The ablation device (1100) may include one or more ECG signal electrodes. For example, one or more electrodes of the second set of electrodes (1130, 1132) may be configured to receive an ECG signal. These ECG signal electrodes, such as the distal tip electrode (1130), may be coupled to its own insulated electrical lead. The ECG signal electrode may be electrically isolated from the inflatable member (1140) using, for example, a ring of

insulation around the ECG signal electrode. In these embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation.

[0109] One or more of a biphasic signal may be applied to the bipole such that tissue may be ablated between the inflatable member (1140) and the first set of electrodes (1120) at a desired location in the ventricle. In some embodiments, the inflatable member (1140) in the second configuration may be configured to contact endocardial tissue while the first set of electrodes (1130) in the second configuration may not contact endocardial tissue. The electric field generated by the ablation device (1100) due to conduction between the inflatable member (1140) and first set of electrodes (1120) through the blood pool and through tissue may result in focal ablation of tissue via irreversible electroporation. The inflatable member (1140) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (1140) is more bulbous than the other end (for example the proximal end) of the inflatable member (1140). The inflatable member (1140) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (1110). In this configuration, the inflatable member (1140) may be contacting an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion).

[0110] In some embodiments, the catheter shaft (1110) may include a deflectable portion between the first set of electrodes (1120) and the second set of electrodes (1130) in the same manner as illustrated in FIG. 3. The deflectable portion may be configured to deflect up to about 210 degrees relative to the longitudinal axis of the catheter shaft (1110). In some embodiments, an actuator (e.g., fluid source) may be coupled to the inflatable member and configured to transition the inflatable member between the first configuration (e.g., deflated state) and the second configuration (e.g., inflated state) by, for example, using pressurized saline.

[0111] FIG. 12 is a side view of another embodiment of an ablation device (1200) (e.g., structurally and/or functionally similar to the ablation device (110, 200, 300, 500, 500', 500'', 500''', 1100) including a catheter shaft (1210) having a first set of electrodes (1220) provided proximal to a second set of electrodes (1230) and an inflatable member (e.g., balloon) (1240). The first set of electrodes (1220) may be formed on a surface of a distal portion of the catheter shaft (1210). That is, the first set of electrodes (1220) may be formed on a surface of the distal

end of the catheter shaft (1210). The second set of electrodes (1230) may be formed on a surface of a distal end of the inflatable member (1240) and may be electrically isolated from the first set of electrodes (1220). In some embodiments, the ablation device (1200) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle. During use, the electrodes (1220, 1230) may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue, as described in more detail herein. A distal portion of the inflatable member (1240) may include and/or be formed in an atraumatic shape that reduces trauma to tissue. The catheter shaft (1210) and inflatable member (1240) may be sized for advancement into an endocardial space (e.g., left ventricle). The catheter shaft (1210) may be flexible so as to be deflectable. For example, a deflectable portion of the catheter shaft (1210) may be configured for deflecting a portion of the catheter (1200) including the second set of electrodes (1230) and the inflatable member (1240) up to about 210 degrees relative to the longitudinal axis. The inflatable member (1240) may be configured to transition between a first configuration (e.g., deflated state) and a second configuration (e.g., inflated state). In the first configuration, the inflatable member (1240) may have a diameter that is about the same as a diameter of the catheter shaft (1210) to aid in advancing the ablation device (1200) through vasculature. For example, the inflatable member (1240) in the first configuration may be approximately parallel to a longitudinal axis of the catheter shaft (1210). The inflatable member (1240) when inflated may bias away from the longitudinal axis. The first set of electrodes (1220) may be structurally and/or functionally similar to the electrodes (220, 230) described with respect to FIGS. 2A-2D.

[0112] The first set of electrodes (1220) may be electrically coupled together using one or more electrical leads. One or more of the second set of electrodes (1230) may be electrically coupled together using a different set of electrical leads. A voltage pulse waveform delivered between the first set of electrodes (1220) and the second set of electrodes (1230) may be used to form a lesion via focal ablation (e.g., a spot lesion) of a predetermined size and shape. In some embodiments, the first set of electrodes (1220) may be configured as an anode while the second set of electrodes (1230) may be configured as a cathode, or vice versa. Accordingly, a bipole may be formed between the first set of electrodes (1220) and the second set of electrodes (1230) that results in an electric field capable of ablating tissue (e.g., myocardial cells on an inner surface or within a ventricle). The second set of electrodes (1230) and the first set of electrodes (1220) may be electrically isolated from each other. For example, the second set of electrodes

(1230) and the first set of electrodes (1220) may each couple to a respective insulated electrical lead, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown.

[0113] The first and second sets of electrodes (1220, 1230) may include an atraumatic shape to reduce trauma to tissue. For example, the first set of electrodes (1220) may be ring electrodes. In some embodiments, the first set of electrodes (1220) may be located along any portion of the catheter shaft (1210) proximal to the second set of electrodes (1230). The first set of electrodes (1220) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode) while allowing the catheter shaft (1210) to remain flexible and facilitate deflection. The second set of electrodes (1230) may be disposed on a surface of the inflatable member (1240) and/or flush with the surface of the inflatable member (1240) so as to be electrically coupled to the inflatable member (1240). The second set of electrodes (1230) may have the same or different sizes, shapes, and/or location along the inflatable member (1240).

[0114] For example, the second set of electrodes (1230) may include a set of generally circular electrodes disposed around a circumference of the inflatable member (1240). In some embodiments, each electrode of the second set of electrodes (1230) may be wired together. In other embodiments, subsets of the electrodes of the second set of electrodes (1230) may be electrically wired together while other subsets may be independently addressable.

[0115] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (1220) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. The ablation device (1200) may include one or more ECG signal electrodes. For example, one or more electrodes of the second set of electrodes (1230) may be configured to receive an ECG signal. These ECG signal electrodes may be coupled to their own insulated electrical lead. In these embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation.

[0116] One or more of a biphasic signal may be applied to the bipole formed by the first set of electrodes (122) and the second sets of electrodes (1230) such that tissue distal to or around the inflatable member (1240) may be ablated at a desired location in the ventricle. For example, a

biphasic pulse waveform may be delivered between the sets of electrodes, resulting in a zone of irreversible electroporation ablation in the region around the inflatable member. The inflatable member (1240) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (1240) is more bulbous than the other end (for example the proximal end) of the inflatable member (1240). The inflatable member (1240) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (1210). In this configuration, the inflatable member (1240) may be placed at an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion). The electrode leads may be configured with sufficient insulation and high dielectric strength to be suitable for delivery of irreversible electroporation energy as described herein.

[0117] In some embodiments, the catheter shaft (1210) may include a deflectable portion between the first set of electrodes (1220) and the second set of electrodes (1230) in some embodiments, or proximal to the first set of electrodes (1220) in other embodiments. The deflectable portion may be configured to deflect up to about 210 degrees relative to the longitudinal axis of the catheter shaft (1210). In some embodiments, an actuator (e.g., fluid source) may be coupled to the inflatable member and configured to transition the inflatable member between the first configuration (e.g., deflated state) and the second configuration (e.g., inflated state) by, for example, using pressurized saline.

[0118] FIG. 13 is a side view of another embodiment of an ablation device (1300) (e.g., structurally and/or functionally similar to the ablation device (110, 200, 300, 500, 500', 500'', 500''', 1100, 1200) including a catheter shaft (1310) having a first set of electrodes (1320) provided proximal to a second set of electrodes (1330, 1332) and an inflatable member (e.g., balloon) (1340). The first set of electrodes (1320) may be formed on a surface of a distal portion of the catheter shaft (1310). That is, the first set of electrodes (1320) may be formed on a surface of the distal end of the catheter shaft (1310). The second set of electrodes (1330, 1332) may be formed on a surface of a distal end of the inflatable member (1340) and may be electrically isolated from the first set of electrodes (1320). In some embodiments, a major axis (e.g., longitudinal axis) of the second electrodes (1332) may be substantially parallel to the longitudinal axis of the catheter shaft (1310) and/or inflatable member (1340).

[0119] In some embodiments, the ablation device (1300) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle. During use, the electrodes (1320, 1330, 1332) may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue, as described in more detail herein. A distal portion of the inflatable member (1340) may include and/or be formed in an atraumatic shape that reduces trauma to tissue. The catheter shaft (1310) and inflatable member (1340) may be sized for advancement into an endocardial space (e.g., left ventricle). The catheter shaft (1310) may be flexible so as to be deflectable. For example, a deflectable portion of the catheter shaft (1310) may be configured for deflecting a portion of the catheter (1300) including the second set of electrodes (1330, 1332) and the inflatable member (1340) up to about 210 degrees relative to the longitudinal axis. The inflatable member (1340) may be configured to transition between a first configuration (e.g., deflated state) and a second configuration (e.g., inflated state). In the first configuration, the inflatable member (1340) may have a diameter that is about the same as a diameter of the catheter shaft (1310) to aid in advancing the ablation device (1300) through vasculature. For example, the inflatable member (1340) in the first configuration may be approximately parallel to a longitudinal axis of the catheter shaft (1310). The inflatable member (1340) when inflated may bias away from the longitudinal axis. The first set of electrodes (1320) may be structurally and/or functionally similar to the electrodes (220, 230) described with respect to FIGS. 2A-2D.

[0120] The first set of electrodes (1320) may be electrically coupled together using one or more electrical leads. The second set of electrodes (1330, 1332) may be electrically coupled together using a different set of electrical leads. A voltage pulse waveform delivered between the first set of electrodes (1320) and the second set of electrodes (1330, 1332) to form a lesion via focal ablation (e.g., a spot lesion) of a predetermined size and shape. In some embodiments, the first set of electrodes (1320) may be configured as an anode while the second set of electrodes (1330, 1332) may be configured as a cathode, or vice versa. The second set of electrodes (1330, 1332) and the first set of electrodes (1320) may be electrically isolated from each other. For example, the second set of electrodes (1330, 1332) and the first set of electrodes (1320) may each couple to a respective insulated electrical lead, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown.

[0121] The first and second sets of electrodes (1320, 1330, 1332) may include an atraumatic shape to reduce trauma to tissue. For example, the first set of electrodes (1320) may be ring electrodes. In some embodiments, the first set of electrodes (1320) may be located along any portion of the catheter shaft (1310) proximal to the second set of electrodes (1330, 1332). The first set of electrodes (1320) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode) while allowing the catheter shaft (1310) to remain flexible and facilitate deflection. The second set of electrodes (1330, 1332) may be disposed on a surface of the inflatable member (1340) and/or flush with the surface of the inflatable member (1340) so as to be electrically coupled to the inflatable member (1340). The second set of electrodes (1330, 1332) may have the same or different sizes, shapes, and/or location along the inflatable member (1340).

[0122] For example, the second set of electrodes (1330, 1332) may include a distal tip electrode (1330) and a set of generally elliptically-shaped electrodes (1332) disposed around a circumference of the inflatable member (1340). For example, the second set of electrodes (1330) may be formed on the inflatable member (1340) on an approximate plane approximately perpendicular to the longitudinal axis. In some embodiments, a longitudinal axis of each of the electrodes (1332) may be substantially parallel to the longitudinal axis of the catheter shaft (1310) and/or inflatable member (1340). In some embodiments, each electrode of the second set of electrodes (1330, 1332) may be wired together. In other embodiments, subsets of the electrodes of the second set of electrodes (1330, 1332) may be electrically wired together while other subsets (e.g., the distal tip electrode) may be independently addressable. In some embodiments, the distal tip electrode (1332) may be electrically isolated from the first set of electrodes (1320). In some embodiments, each electrode of the second set of electrodes (1330, 1332) may be independently addressable. The distal tip electrode (1330) may be formed at a distal portion of the inflatable member (1340) and electrically isolated from the first set of electrodes (1320).

[0123] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (1320, 1330, 1332) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. The ablation device (1300) may include one or more ECG signal electrodes. For example, one or more electrodes of the second set of electrodes (1330, 1332) may be configured to receive an ECG signal. These ECG signal electrodes, such as the

distal tip electrode (1330), may be coupled to its own insulated electrical lead. In these embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation.

[0124] The inflatable member (1340) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (1340) is more bulbous than the other end (for example the proximal end) of the inflatable member (1340). The inflatable member (1340) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (1310). In this configuration, the inflatable member (1340) may be placed at an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion). The electrode leads may be configured with sufficient insulation and high dielectric strength to be suitable for delivery of irreversible electroporation energy as described herein.

[0125] In some embodiments, the catheter shaft (1310) may include a deflectable portion between the first set of electrodes (1320) and the second set of electrodes (1330), or proximal to the first set of electrodes (1320). The deflectable portion may be configured to deflect up to about 210 degrees relative to the longitudinal axis of the catheter shaft (1310). In some embodiments, an actuator (e.g., fluid source) may be coupled to the inflatable member and configured to transition the inflatable member between the first configuration (e.g., deflated state) and the second configuration (e.g., inflated state) by, for example, using pressurized saline.

[0126] FIG. 14 is a side view of another embodiment of an ablation device (1400) (e.g., structurally and/or functionally similar to the ablation device (110, 200, 300, 500, 500', 500'', 500''', 1100, 1200, 1300) including a catheter shaft (1410) having a first set of electrodes (1420) provided proximal to a second set of electrodes (1430, 1432) and an inflatable member (e.g., balloon) (1440). The first set of electrodes (1420) may be formed on a surface of a proximal portion of the inflatable member (1440). For example, the first set of electrodes (1420) may be formed proximal to an equatorial plane of the inflatable member (1440). As used herein, the equatorial plane of the inflatable member (1440) refers to the plane intersecting the maximum cross-sectional diameter of the inflatable member (1440) when inflated. That is, a proximal portion of the inflatable member (1440) is proximal to a cross-sectional diameter of the inflatable member (1440) at its largest portion. The second set of electrodes (1430, 1432) may be

formed on a surface of the inflatable member (1440) distal to the equatorial plane and may be electrically isolated from the first set of electrodes (1420). In some embodiments, a major axis (e.g., longitudinal axis) of the first set of electrodes (1420) and the second set of electrodes (1432) may be substantially parallel to the longitudinal axis of the catheter shaft (1410) and/or inflatable member (1440).

[0127] In some embodiments, the ablation device (1400) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle. During use, the electrodes (1420, 1430, 1432) may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue, as described in more detail herein. A distal portion of the inflatable member (1440) may include and/or be formed in an atraumatic shape that reduces trauma to tissue. The catheter shaft (1410) and inflatable member (1440) may be sized for advancement into an endocardial space (e.g., left ventricle). The catheter shaft (1410) may be flexible so as to be deflectable. For example, a deflectable portion of the catheter shaft (1410) may be configured for deflecting a portion of the catheter (1400) including first set of electrodes (1420) and the second set of electrodes (1430, 1432) and the inflatable member (1440) up to about 210 degrees relative to the longitudinal axis. The inflatable member (1440) may be configured to transition between a first configuration (e.g., deflated state) and a second configuration (e.g., inflated state). In the first configuration, the inflatable member (1440) may have a diameter that is about the same as a diameter of the catheter shaft (1410) to aid in advancing the ablation device (1400) through vasculature. For example, the inflatable member (1440) in the first configuration may be approximately parallel to a longitudinal axis of the catheter shaft (1410). The inflatable member (1440) when inflated may bias away from the longitudinal axis.

[0128] The first set of electrodes (1420) may be electrically coupled together using one or more electrical leads. The second set of electrodes (1430, 1432) may be electrically coupled together using a different set of electrical leads. Accordingly, a bipole may be formed between the first set of electrodes (1420) and the second set of electrodes (1430, 1432) that results in an electric field capable of ablating tissue (e.g., myocardial cells on an inner surface or within a ventricle). For example, the second set of electrodes (1430, 1432) and the first set of electrodes (1420) may each couple to a respective insulated electrical lead, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown.

[0129] The first and second sets of electrodes (1420, 1430, 1432) may include an atraumatic shape to reduce trauma to tissue. For example, the first set of electrodes (1420) may have a set of generally elliptically-shaped electrodes (1420) disposed around a circumference of the inflatable member (1440). In some embodiments, the first set of electrodes (1420) may be located along any portion of the inflatable member (1440) proximal to the second set of electrodes (1430, 1432). The first set of electrodes (1420) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode). The second set of electrodes (1430, 1432) may be disposed on a distal end of the inflatable member (1430, 1432) and electrically isolated from the first set of electrodes (1420).

[0130] The first and second set of electrodes (1420, 1430, 1432) may have the same or different sizes, shapes, and/or location along the inflatable member (1440). For example, one or more electrodes of the first and second set of electrodes (1420, 1430, 1432) may have a generally elliptical shape. For example, the second set of electrodes (1430, 1432) may include a distal tip electrode (1430) and a set of generally elliptically-shaped electrodes (1432) disposed around a circumference of the inflatable member (1440). In some embodiments, a longitudinal axis of each of the electrodes (1420, 1432) may be substantially parallel to the longitudinal axis of the catheter shaft (1410) and/or inflatable member (1440). In some embodiments, each electrode of the second set of electrodes (1430, 1432) may be wired together. In other embodiments, subsets of the electrodes of the second set of electrodes (1430, 1432) may be electrically wired together while other subsets (e.g., the distal tip electrode) may be independently addressable. In some embodiments, the distal tip electrode (1432) may be electrically isolated from the first set of electrodes (1420). In some embodiments, one or more electrodes of the first and second set of electrodes (1420, 1430, 1432) may be independently addressable. The distal tip electrode (1430) may be formed at a distal portion of the inflatable member (1440).

[0131] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (1420, 1430, 1432) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. The ablation device (1400) may include one or more ECG signal electrodes. For example, one or more electrodes of the second set of electrodes (1430, 1432) may be configured to receive an ECG signal. These ECG signal electrodes, such as the distal tip electrode (1430), may be coupled to its own insulated electrical lead. In these

embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation.

[0132] In some embodiments, the first and second set of electrodes (1420, 1430, 1432) may be configured to deliver a pulse waveform from a signal generator to tissue during use. The inflatable member (1440) may be coupled to a distal portion of the catheter shaft (1410) and configured for delivery of irreversible electroporation energy to tissue. The first set of electrodes (1420) and the second set of electrodes (1430, 1432) may have opposite electrical polarities during delivery of a pulse waveform.

[0133] The electric field generated by the ablation device (1400) due to conduction between the second set of electrodes (1430, 1432) and the first set of electrodes (1420) through the blood pool and through tissue may result in focal ablation of tissue via irreversible electroporation. The inflatable member (1440) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (1440) is more bulbous than the other end (for example the proximal end) of the inflatable member (1440). The inflatable member (1440) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (1410). In this configuration, the inflatable member (1440) may be placed at an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion). The electrode leads may be configured with sufficient insulation and high dielectric strength to be suitable for delivery of irreversible electroporation energy as described herein.

[0134] In some embodiments, the catheter shaft (1410) may include a deflectable portion such as in a distal portion of the catheter shaft (1410). The deflectable portion may be configured to deflect up to about 210 degrees relative to the longitudinal axis of the catheter shaft (1410). In some embodiments, an actuator (e.g., fluid source) may be coupled to the inflatable member and configured to transition the inflatable member between the first configuration (e.g., deflated state) and the second configuration (e.g., inflated state) by, for example, using pressurized saline.

[0135] FIG. 15 is a side view of another embodiment of an ablation device (1500) (e.g., structurally and/or functionally similar to the ablation device (110, 200, 300, 500, 500', 500'', 500''', 1100, 1200, 1300, 1400) including a catheter shaft (1510) having a first set of electrodes (1520) provided proximal to a second set of electrodes (1530, 1532, 1534) and an inflatable

member (e.g., balloon) (1540). The first set of electrodes (1510) may be formed on a surface of a distal portion of the catheter shaft (1510). That is, the first set of electrodes (1520) may be formed on a surface of the distal end of the catheter shaft (1510). The second set of electrodes (1530, 1532, 1534) may be formed on a surface of the inflatable member (1540) and may be electrically isolated from the first set of electrodes (1520). In some embodiments, a major axis (e.g., longitudinal axis) of the second electrodes (1532, 1534) may be substantially parallel to the longitudinal axis of the catheter shaft (1510) and/or inflatable member (1540).

[0136] In some embodiments, the ablation device (1500) is useful for forming lesions on endocardial surfaces via focal ablation, such as an inner surface of a ventricle. During use, the electrodes (1520, 1530, 1532, 1534) may be disposed in a ventricle in order to deliver a pulse waveform to ablate tissue, as described in more detail herein. A distal portion of the inflatable member (1540) may include and/or be formed in an atraumatic shape that reduces trauma to tissue. The catheter shaft (1510) and inflatable member (1540) may be sized for advancement into an endocardial space (e.g., left ventricle). The catheter shaft (1510) may be flexible so as to be deflectable. For example, a deflectable portion of the catheter shaft (1510) may be configured for deflecting a portion of the catheter (1500) including the second set of electrodes (1530, 1532, 1534) and the inflatable member (1540) up to about 210 degrees relative to the longitudinal axis. The inflatable member (1540) may be configured to transition between a first configuration (e.g., deflated state) and a second configuration (e.g., inflated state). In the first configuration, the inflatable member (1540) may have a diameter that is about the same as a diameter of the catheter shaft (1510) to aid in advancing the ablation device (1500) through vasculature. For example, the inflatable member (1540) in the first configuration may be approximately parallel to a longitudinal axis of the catheter shaft (1510). The inflatable member (1540) when inflated may bias away from the longitudinal axis. The first set of electrodes (1520) may be structurally and/or functionally similar to the electrodes (220, 230) described with respect to FIGS. 2A-2D.

[0137] The first set of electrodes (1520) may be electrically coupled together using one or more electrical leads. The proximal electrodes (1534) of the second set of electrodes and the distal electrodes (1532, 1530) of the second set of electrodes may be electrically wired respectively separately using different sets of electrical leads. In some embodiments, the first set of electrodes (1520) may be configured as an anode while the second set of electrodes (1530, 1532, 1534) may be configured as a cathode, or vice versa. In alternate embodiments, the first

set of electrodes (1520) and the proximal electrodes (1534) of the second set of electrodes may be configured as an anode while the distal electrodes (1532, 1530) of the second set of electrodes may be configured as a cathode, or vice versa. For example, the proximal electrodes (1534) of the second set of electrodes, the distal electrodes (1532, 1530) of the second set of electrodes, and the first set of electrodes (1520) may each couple to respective insulated electrical leads, with each lead having sufficient electrical insulation to sustain an electrical potential difference of at least 700 V across its thickness without dielectric breakdown.

[0138] The first and second sets of electrodes (1520, 1530, 1532, 1534) may include an atraumatic shape to reduce trauma to tissue. For example, the first set of electrodes (1520) may be ring electrodes. In some embodiments, the first set of electrodes (1520) may be located along any portion of the catheter shaft (1510) proximal to the second set of electrodes (1530, 1532, 1534). The first set of electrodes (1520) may be spaced apart from each other and wired together via one or more insulated leads so as to function as a single electrode (e.g., anode or cathode) while allowing the catheter shaft (1510) to remain flexible and facilitate deflection. The second set of electrodes (1530, 1532, 1534) may be disposed on a surface of the inflatable member (1540) and/or flush with the surface of the inflatable member (1540). The second set of electrodes (1530, 1532) may have the same or different sizes, shapes, and/or location along the inflatable member (1540).

[0139] For example, the second set of electrodes (1530, 1532, 1534) may include a distal tip electrode (1530) and a set of generally elliptically-shaped electrodes (1532, 1534) disposed around a circumference of the inflatable member (1540). In some embodiments, a major axis (e.g., longitudinal axis) of each of the electrodes (1532, 1534) may be substantially parallel to the longitudinal axis of the catheter shaft (1510) and/or inflatable member (1540). In some embodiments, the distal tip electrode (1532) may be electrically isolated from the first set of electrodes (1520). In some embodiments, each electrode of the second set of electrodes (1530, 1532, 1534) may be independently addressable. The distal tip electrode (1530) may be formed at a distal portion of the inflatable member (1540) and electrically isolated from the first set of electrodes (1520).

[0140] In some embodiments, a set of the second set of electrodes may be electrically coupled with the first set of electrodes. For example, the first set of electrodes (1520) and the proximal

electrodes (1534) of the second set of electrodes may be electrically coupled together using one or more electrical leads. In some embodiments, the proximal electrodes (1534) may be formed proximal to a maximum cross-sectional diameter of the inflatable member (1540) when inflated. That is, a proximal portion of the inflatable member (1540) is proximal to a cross-sectional diameter of the inflatable member (1540) at its largest portion. In this configuration the distal electrodes (1530, 1532) of the second set of electrodes may be configured to contact tissue in the second configuration while the first set of electrodes (1520) and the proximal electrodes (1534) of the second set of electrodes may be configured for non-contact with tissue in the second configuration.

[0141] In some embodiments, one or more of the electrodes of the first and second sets of electrodes (1520, 1530, 1532, 1534) may be configured for receiving or sensing an ECG signal for recording electrophysiology data. The ablation device (1500) may include one or more ECG signal electrodes. For example, one or more electrodes of the second set of electrodes (1530, 1532, 1534) may be configured to receive an ECG signal. These ECG signal electrodes, such as the distal tip electrode (1530), may be coupled to its own insulated electrical lead. In these embodiments, the ablation device may be used to record electrophysiology data in place of a mapping catheter before and/or after tissue ablation.

[0142] The inflatable member (1540) when inflated may have an asymmetric shape in a proximal-to-distal direction, so that one end (for example the distal end) of the inflatable member (1540) is more bulbous than the other end (for example the proximal end) of the inflatable member (1540). The inflatable member (1540) when inflated may be rotationally symmetric about the longitudinal axis of the catheter shaft (1510). In this configuration, the inflatable member (1540) may be placed at an endocardial surface and used to form a lesion via focal ablation (e.g., a spot lesion). The electrode leads may be configured with sufficient insulation and high dielectric strength to be suitable for delivery of irreversible electroporation energy as described herein.

[0143] In some embodiments, the catheter shaft (1510) may include a deflectable portion between the first set of electrodes (1520) and the second set of electrodes (1530). In other embodiments the deflectable portion may be proximal to the first set of electrodes (1520). The deflectable portion may be configured to deflect up to about 210 degrees relative to the

longitudinal axis of the catheter shaft (1510). In some embodiments, an actuator (e.g., fluid source) may be coupled to the inflatable member and configured to transition the inflatable member between the first configuration (e.g., deflated state) and the second configuration (e.g., inflated state) by, for example, using pressurized saline.

[0144] In the embodiments described herein with respect to FIGS. 11-15, the first set of electrodes may be spaced apart from the second set of electrodes by between about 2 mm and about 10 mm. In some embodiments, the first set of electrodes may be formed on a portion of the catheter shaft having a length of between about 2 mm and about 12 mm. In some embodiments, the inflatable member when inflated may have a shape with an effective cross-sectional diameter at its largest portion of between about 5 mm and about 15 mm. In some embodiments, the inflatable member may have a length of up to about 22 mm. For example, the inflatable member may have substantially the same length in the first configuration and the second configuration. In some embodiments, one or more electrodes of the first set of electrodes may have a width of between about 1 mm and about 5 mm and may be spaced apart by between about 1 mm and about 5 mm. In some embodiments, a distal-most electrode of the first set of electrodes may be spaced apart by at least about 5 mm from a proximal end of the inflatable member when inflated.

II. Methods

[0145] Also described here are methods for ablating tissue in a heart chamber using the systems and devices described above. The heart chamber may include one or more of the right, left ventricle, and/or right, left atria. Generally, the methods described here include introducing and disposing a device in contact with one or more chambers such as the ventricles. A pulse waveform may be delivered by one or more electrodes and an inflatable member (e.g., balloon) of the device to ablate tissue. In some embodiments, a cardiac pacing signal may synchronize the delivered pulse waveforms with the cardiac cycle. Additionally or alternatively, the pulse waveforms may include a plurality of levels of a hierarchy to reduce total energy delivery. The tissue ablation thus performed may be delivered in synchrony with paced heartbeats and with less energy delivery to reduce damage to healthy tissue. It should be appreciated that any of the ablation devices described herein may be used to ablate tissue using the methods discussed below as appropriate.

[0146] In some embodiments, the ablation devices described herein may be used for focal ablation of cardiac features/structures identified to cause arrhythmia. For example, a cardiac electrophysiology diagnostic catheter (e.g., mapping catheter) may be used to map cardiac structures such as re-entrant circuits and ventricular scar tissue that may be subsequently ablated through focal ablation using any of the ablation devices described herein. Focal ablation may, for example, create a spot lesion that neutralizes a re-entrant circuit while sparing surrounding tissue. In some embodiments, one or more focal ablation lesions may be formed in combination with one or more box or line lesions to treat cardiac arrhythmia. As a non-limiting example, in some embodiments, a system can include one or more mapping catheters, one or more ablation devices (e.g., as illustrated in FIGS. 2A-2C and 3) useful for creating lesions via focal ablation.

[0147] Generally, and as illustrated in FIGS. 4A-4B, a method (400) includes the introduction of a device (e.g., ablation device, such as the ablation devices (110, 200, 300, 500, 500', 500'', 500''', 1100, 1200, 1300, 1400, 1500)) into an endocardial space of a ventricle. The ablation device may be introduced in a first configuration and transitioned to a second configuration in the ventricle. Once positioned in the ventricle, voltage pulse waveforms may be applied to tissue during a refractory period of the cardiac cycle. Electrophysiology data of the ventricle may be recorded to determine efficacy of the ablation.

[0148] The method (400) may begin with creating an access site in a patient (402). For example, to access the left ventricle for treatment, an antegrade delivery approach may be used, in which the first access site may be via a femoral vein of the patient. A guidewire may be advanced into the access site via the femoral vein and into the right atrium of the patient (404). A dilator and a deflectable sheath may be advanced over the guidewire and into the right atrium (406). The sheath may, for example, be configured for deflecting up to about 210 degrees. The dilator may be advanced from the right atrium into the left atrium through the septum (408) to create a transseptal opening. For example, the dilator may be advanced from the right atrium into the left atrium through the interatrial septum to create the transseptal opening. The interatrial septum may include the fossa ovalis of the patient. The transseptal opening may be dilated using the dilator (410). For example, the dilator may be advanced out of the sheath and used to poke the fossa ovalis to create the transseptal opening (assuming the patient is heparinized). Alternatively, a transseptal needle (e.g., Brockenbrough needle) may be used to create the transseptal opening. The sheath may be advanced from the right atrium into the left atrium (412)

through the transseptal opening. An ablation device may be advanced into the left ventricle over the guidewire (414) via the mitral valve. Alternatively, the left ventricle may be accessed by a retrograde approach, in which the first access site may be via a femoral artery of the patient, and a guidewire and ablation device may be advanced through an aorta of the patient, and then through the aortic valve into the left ventricle. For treatment of the right ventricle, the first access site may again be via a femoral vein of the patient, and the guidewire and ablation device may be advanced into the right atrium of the patient and then through the tricuspid valve into the right ventricle.

[0149] In some embodiments, the ablation device may include a catheter shaft lumen and a set of insulated electrical leads extending through the shaft lumen. The catheter shaft may include one or more electrodes formed on a surface of the shaft. In some embodiments, one or more electrodes may be disposed on one or more portions of the inflatable member. For example, an electrode may be disposed on a distal end of the inflatable member. One or more of the electrodes may be configured to receive electrophysiology signals from the ventricle. In the method of FIGS. 4A-4B, an ablation device may be configured to record electrophysiology data of the ventricle. In some embodiments, to allow the ablation device to record electrophysiology data, the ablation device may be transitioned from the first configuration into the second configuration (416) within the ventricle (e.g., left ventricle). In some embodiments, the inflatable member may be transitioned between the first and second configurations using a handle of the ablation device. For example, the handle may include a saline flow control mechanism to control a volume of saline within an inflatable member. The handle may further include a saline volume indicator to indicate a configuration of the inflatable member. The ablation device in the second configuration may be configured to record electrophysiology data using the ablation device (418). For example, one or more electrodes on the catheter shaft and inflatable member may be configured for receiving an ECG signal for recording electrophysiology data.

[0150] In other embodiments, a separate diagnostic device (e.g., a mapping catheter) may be used to record electrophysiology data of the ventricle to be treated. Electrophysiology data may be used to generate an anatomical map that may be used to compare electrophysiology data recorded after energy delivery (e.g., ablation). The diagnostic device may be advanced into the selected ventricle via a femoral vein or jugular vein. In these embodiments, the diagnostic device (e.g., second catheter) may be advanced into the right ventricle (via the tricuspid valve) or

into the ventricle (via the left atrium and the mitral valve) over the guidewire after step (412) instead of advancing the ablation device into the selected ventricle. The second catheter may be used to record electrophysiology data of one or more ventricles. Once completed, the diagnostic device may be withdrawn from the body over the guidewire, and the ablation device may then be advanced over the guidewire into the selected ventricle.

[0151] Still referring to FIGS. 4A-4B, a second access site may be created in the patient to advance a lead or catheter for cardiac stimulation into the patient's heart. For example, the second access site may be via a jugular vein of the patient. The device for cardiac stimulation may be advanced into the right ventricle through the second access site (420) (e.g., near the apex of the right ventricle). A pacing signal may be generated by a cardiac stimulator and applied to the heart for cardiac stimulation of the heart. An indication of the pacing signal may be transmitted from the cardiac stimulator to the signal generator. In some embodiments, the operator may confirm the pacing capture and determine that the ventricle is responding to the pacing signal as intended. For example, pacing capture may be confirmed on an ECG display on a signal generator. Confirmation of pacing capture is a safety feature in that ablation is delivered in synchrony with pacing through enforced periodicity of a Q-wave through pacing.

[0152] The ablation device may be advanced towards a target ventricle (422) for delivering a pulse waveform configured for tissue ablation. In particular, the ablation device in the second configuration may be advanced towards a ventricle of the heart to contact a tissue surface. The sheath may be deflected as needed to direct the ablation device towards the target ventricle. The inflatable member may be transitioned to a second configuration where the inflatable member inflates to contact the inflatable member against the ventricle at a predetermined location. Once the ablation device is in position within the heart to deliver one or more pulse waveforms, an extension cable may be used to electrically couple a signal generator to a proximal end of the handle of the ablation device. After pacing the right ventricle using the pacing device (424), the pulse waveform may be delivered to the ventricle using the ablation device to ablate tissue in a portion of the target ventricle (426). The pulse waveform may be delivered in synchronization with the pacing signal.

[0153] As described in detail in the figures (e.g., FIGS. 5A-5J), the ablation device may be configured to generate an electric field intensity in a region of myocardial tissue of a ventricle

(e.g., where there may be re-entrant circuits, etc.) that is large enough to cause irreversible electroporation in tissue. For example, the inflatable member of the ablation device in FIG. 5D may be in contact with a tissue surface and may be used to generate a set of high intensity electric field lines that penetrate the ventricle at a depth of between about 5 mm to about 8 mm or more to form one or more focal ablation lesions, as shown by the spatial zone (532) in FIG. 5E. The ablation zone corresponding to the spatial region (532) may be wide and deep. The size of the inflatable member may be modified to control a depth and strength of the electric field. This allows energy to be delivered more efficiently and thus permits tissue ablation with minimal total energy delivered.

[0154] While examples of ablation devices configured for delivery of irreversible electroporation pulsed electric field therapy have been described here, the examples described herein are provided for exemplary purposes only and those skilled in the art may devise other variations without departing from the scope of the present invention. For example, a range and variety of materials, polyhedral sides, electrode diameters, device dimensions, voltage levels, proximal electrodes, and other such details are possible and may be implemented as convenient for the application at hand without departing from the scope of the present invention. The catheter shaft may undergo a range of deflections by controlling deflection from a catheter handle. The metallized electrode portions disposed on the inflatable member embodiments may be used for ECG signal recording or irreversible electroporation therapy delivery or both.

[0155] As discussed herein, the pulse waveform may be generated by a signal generator coupled to the ablation device. The signal generator may be electrically coupled to a proximal end of a handle of the ablation device. For example, an extension cable may electrically couple the signal generator to the proximal end of the handle. In some embodiments, the pulse waveform may include a time offset with respect to the pacing signal. In some embodiments, the pulse waveform may include a first level of a hierarchy of the pulse waveform including a first set of pulses. Each pulse has a pulse time duration and a first time interval separating successive pulses. A second level of the hierarchy of the pulse waveform may include a plurality of first sets of pulses as a second set of pulses. A second time interval may separate successive first sets of pulses. The second time interval may be at least three times the duration of the first time interval. A third level of the hierarchy of the pulse waveform may include a plurality of second sets of pulses as a third set of pulses. A third time interval may separate successive second sets

of pulses. The third time interval may be at least thirty times the duration of the second level time interval. A fourth level of the hierarchy of the pulse waveform may include a plurality of third sets of pulses as a fourth set of pulses. A fourth time interval may separate successive third sets of pulses. The fourth time interval may be at least ten times the duration of the third level time interval.

[0156] One or more electrodes of the ablation device in the second configuration may be configured to receive electrophysiology signals of the target ventricle and used to record electrophysiology data of the target ventricle (428). The electrophysiology data may be compared to the baseline data recorded prior to ablation to determine if ablation was successful (430).

[0157] In other embodiments, the ablation device may be withdrawn from the heart over the guidewire and a mapping catheter may be advanced over the guidewire to record the post-ablation electrophysiology data of the target ventricle. If the ablation is not successful (430 – NO) based on the electrophysiology data and predetermined criteria, then the process may return to step 426 for delivery of additional pulse waveforms. The pulse waveform parameters may be the same or changed for subsequent ablation cycles.

[0158] If analysis of the electrophysiology data indicates that the ablation of a ventricle portion is successful (e.g., tissue portion is electrically silent) (430 - YES), then a determination may be made of other target ventricle portions to ablate (432). Another target ventricle portion may be selected (424) and the process may return to step 422 when other ventricular portions are to be ablated. When switching between target ventricles, the inflatable member may be at least partially deflated, and the ablation device may be advanced towards another portion of tissue. If no other portions are to be ablated (432 – NO), the ablation device, cardiac stimulator, sheath, guidewire, and the like, may be removed from the patient (436).

[0159] In other embodiments, the diagnostic device (e.g., mapping catheter) may be used to record electrophysiology data of the ventricle after pulse waveforms are delivered to tissue by the ablation device. In these embodiments, the ablation device may be withdrawn from the patient over the guidewire after steps 426 or 436 and the diagnostic device may be advanced into

the ventricle over the guidewire to record electrophysiology data of the target ventricle having undergone tissue ablation.

[0160] It should be noted that for any of the steps described herein, a radiopaque portion of the ablation device may be fluoroscopically imaged to aid an operator. For example, visual confirmation may be performed through fluoroscopic imaging that the inflatable members in the second configuration is in contact with the ventricle or to visually confirm an apposition of the inflatable member and electrodes relative to the ventricle. Imaging from a plurality of angles may be used to confirm positioning.

[0161] It should be understood that the examples and illustrations in this disclosure serve exemplary purposes and departures and variations such as inflatable member characteristics, number of electrodes, and so on can be built and deployed according to the teachings herein without departing from the scope of this invention.

Pulse Waveform

[0162] Disclosed herein are methods, systems and apparatuses for the selective and rapid application of pulsed electric fields/waveforms to effect tissue ablation with irreversible electroporation. The pulse waveform(s) as disclosed herein are usable with any of the systems (100), devices (e.g., 200, 300), and methods (e.g., 400) described herein. Some embodiments are directed to pulsed high voltage waveforms together with a sequenced delivery scheme for delivering energy to tissue via sets of electrodes. In some embodiments, peak electric field values can be reduced and/or minimized while at the same time sufficiently large electric field magnitudes can be maintained in regions where tissue ablation is desired. In some embodiments, a system useful for irreversible electroporation includes a signal generator and a processor capable of being configured to apply pulsed voltage waveforms to a selected plurality or a subset of electrodes of an ablation device. In some embodiments, the processor is configured to control inputs whereby selected pairs of anode-cathode subsets of electrodes can be sequentially triggered based on a pre-determined sequence, and in one embodiment the sequenced delivery can be triggered from a cardiac stimulator and/or pacing device. In some embodiments, the ablation pulse waveforms are applied in a refractory period of the cardiac cycle so as to avoid disruption of the sinus rhythm of the heart. One example method of enforcing this is to electrically pace the heart with a cardiac stimulator and ensure pacing capture to establish

periodicity and predictability of the cardiac cycle, and then to define a time window well within the refractory period of this periodic cycle within which the ablation waveform is delivered.

[0163] In some embodiments, the pulsed voltage waveforms disclosed herein are hierarchical in organization and have a nested structure. In some embodiments, the pulsed waveform includes hierarchical groupings of pulses with a variety of associated timescales. Furthermore, the associated timescales and pulse widths, and the numbers of pulses and hierarchical groupings, can be selected so as to satisfy one or more of a set of Diophantine inequalities involving the frequency of cardiac pacing.

[0164] Pulsed waveforms for electroporation energy delivery as disclosed herein may enhance the safety, efficiency and effectiveness of the energy delivery by reducing the electric field threshold associated with irreversible electroporation, yielding more effective ablative lesions with reduced total energy delivered. This in turn can broaden the areas of clinical application of electroporation including therapeutic treatment of a variety of cardiac arrhythmias.

[0165] FIG. 6 illustrates a pulsed voltage waveform in the form of a sequence of rectangular double pulses, with each pulse, such as the pulse (600) being associated with a pulse width or duration. The pulse width/duration can be about 0.5 microseconds, about 1 microsecond, about 5 microseconds, about 10 microseconds, about 25 microseconds, about 50 microseconds, about 100 microseconds, about 125 microseconds, about 140 microseconds, about 150 microseconds, including all values and sub-ranges in between. The pulsed waveform of FIG. 6 illustrates a set of monophasic pulses where the polarities of all the pulses are the same (all positive in FIG. 6, as measured from a zero baseline). In some embodiments, such as for irreversible electroporation applications, the height of each pulse (600) or the voltage amplitude of the pulse (600) can be in the range from about 400 volts, about 1,000 volts, about 5,000 volts, about 10,000 volts, about 15,000 volts, including all values and sub ranges in between. As illustrated in FIG. 6, the pulse (600) is separated from a neighboring pulse by a time interval (602), also sometimes referred to as a first time interval. The first time interval can be about 3 microseconds, about 50 microseconds, about 100 microseconds, about 200 microseconds, about 500 microseconds, about 800 microseconds, about 1 millisecond including all values and sub ranges in between, in order to generate irreversible electroporation.

[0166] FIG. 7 introduces a pulse waveform with the structure of a hierarchy of nested pulses. FIG. 7 shows a series of monophasic pulses such as pulse (700) with pulse width/pulse time duration w , separated by a time interval (also sometimes referred to as a first time interval) such as (702) of duration t_1 between successive pulses, a number m_1 of which are arranged to form a group of pulses (710) (also sometimes referred to as a first set of pulses). Furthermore, the waveform has a number m_2 of such groups of pulses (also sometimes referred to as a second set of pulses) separated by a time interval (712) (also sometimes referred to as a second time interval) of duration t_2 between successive groups. The collection of m_2 such pulse groups, marked by (720) in FIG. 7, constitutes the next level of the hierarchy, which can be referred to as a packet and/or as a third set of pulses. The pulse width and the time interval t_1 between pulses can both be in the range of microseconds to hundreds of microseconds, including all values and sub ranges in between. In some embodiments, the time interval t_2 can be at least three times larger than the time interval t_1 . In some embodiments, the ratio t_2/t_1 can be in the range between about 3 and about 300, including all values and sub-ranges in between.

[0167] FIG. 8 further elaborates the structure of a nested pulse hierarchy waveform. In this figure, a series of m_1 pulses (individual pulses not shown) form a group of pulses (800) (e.g., a first set of pulses). A series of m_2 such groups separated by an inter-group time interval (810) of duration t_2 (e.g., a second time interval) between one group and the next form a packet (e.g., a second set of pulses). A series of m_3 such packets separated by time intervals (812) of duration t_3 (e.g., a third time interval) between one packet and the next form the next level in the hierarchy, a super-packet labeled (820) (e.g., a third set of pulses) in the figure. In some embodiments, the time interval t_3 can be at least about thirty times larger than the time interval t_2 . In some embodiments, the time interval t_3 can be at least fifty times larger than the time interval t_2 . In some embodiments, the ratio t_3/t_2 can be in the range between about 30 and about 800, including all values and sub-ranges in between. The amplitude of the individual voltage pulses in the pulse hierarchy can be anywhere in the range from 500 volts to 7,000 volts or higher, including all values and sub ranges in between.

[0168] FIG. 9 provides an example of a biphasic waveform sequence with a hierarchical structure. In the example shown in the figure, biphasic pulses such as (900) have a positive voltage portion as well as a negative voltage portion to complete one cycle of the pulse. There is a time delay (902) (e.g., a first time interval) between adjacent cycles of duration t_1 , and n_1 such

cycles form a group of pulses (910) (e.g., a first set of pulses). A series of n_2 such groups separated by an inter-group time interval (912) (e.g., a second time interval) of duration t_2 between one group and the next form a packet (920) (e.g., a second set of pulses). The figure also shows a second packet (930), with a time delay (932) (e.g., a third time interval) of duration t_3 between the packets. Just as for monophasic pulses, higher levels of the hierarchical structure can be formed as well. The amplitude of each pulse or the voltage amplitude of the biphasic pulse can be anywhere in the range from 500 volts to 7,000 volts or higher, including all values and sub ranges in between. The pulse width/pulse time duration can be in the range from nanoseconds or even sub-nanoseconds to tens of microseconds, while the delays t_1 can be in the range from zero to several microseconds. The inter-group time interval t_2 can be at least ten times larger than the pulse width. In some embodiments, the time interval t_3 can be at least about twenty times larger than the time interval t_2 . In some embodiments, the time interval t_3 can be at least fifty times larger than the time interval t_2 .

[0169] Embodiments disclosed herein include waveforms structured as hierarchical waveforms that include waveform elements/pulses at various levels of the hierarchy. The individual pulses such as (700) in FIG. 7 comprise the first level of the hierarchy, and have an associated pulse time duration and a first time interval between successive pulses. A set of pulses, or elements of the first level structure, form a second level of the hierarchy such as the group of pulses/second set of pulses (710) in FIG. 7. Among other parameters, associated with the waveform are parameters such as a total time duration of the second set of pulses (not shown), a total number of first level elements/first set of pulses, and second time intervals between successive first level elements that describe the second level structure/second set of pulses. In some embodiments, the total time duration of the second set of pulses can be between about 20 microseconds and about 10 milliseconds, including all values and subranges in between. A set of groups, second set of pulses, or elements of the second level structure, form a third level of the hierarchy such as the packet of groups/third set of pulses (720) in FIG. 7. Among other parameters, there is a total time duration of the third set of pulses (not shown), a total number of second level elements/second set of pulses, and third time intervals between successive second level elements that describe the third level structure/third set of pulses. In some embodiments, the total time duration of the third set of pulses can be between about 60 microseconds and about 200 milliseconds, including all values and sub ranges in between. The

generally iterative or nested structure of the waveforms can continue to a higher plurality of levels, such as ten levels of structure, or more.

[0170] For example, a pulse waveform may include a fourth level of the hierarchy of the pulse waveform may include a plurality of third sets of pulses as a fourth set of pulses, a fourth time interval separating successive third sets of pulses, the fourth time interval being at least ten times the duration of the third level time interval.

[0171] In some embodiments, hierarchical waveforms with a nested structure and hierarchy of time intervals as described herein are useful for irreversible electroporation ablation energy delivery, providing a good degree of control and selectivity for applications in different tissue types. A variety of hierarchical waveforms can be generated with a suitable pulse generator. It is understood that while the examples herein identify separate monophasic and biphasic waveforms for clarity, it should be noted that combination waveforms, where some portions of the waveform hierarchy are monophasic while other portions are biphasic, can also be generated/implemented.

[0172] In some embodiments, the ablation pulse waveforms described herein are applied during the refractory period of the cardiac cycle so as to avoid disruption of the sinus rhythm of the heart. In some embodiments, a method of treatment includes electrically pacing the heart with a cardiac stimulator to ensure pacing capture to establish periodicity and predictability of the cardiac cycle, and then defining a time window within the refractory period of the cardiac cycle within which one or more pulsed ablation waveforms can be delivered. FIG. 10 illustrates an example where both atrial and ventricular pacing is applied (for instance, with pacing leads or catheters situated in the right atrium and right ventricle respectively). With time represented on the horizontal axis, FIG. 10 illustrates a series of ventricular pacing signals such as (1000) and (1010), and a series of atrial pacing signals (1020, 1030), along with a series of ECG waveforms (1040, 1042) that are driven by the pacing signals. As indicated in FIG. 10 by the thick arrows, there is an atrial refractory time window (1022) and a ventricular refractory time window (1002) that respectively follow the atrial pacing signal (1022) and the ventricular pacing signal (1000). As shown in FIG. 10, a common refractory time window (1050) of duration T_r can be defined that lies within both atrial and ventricular refractory time windows (1022, 1002). In some embodiments, the electroporation ablation waveform(s) can be applied in this common

refractory time window (1050). The start of this refractory time window (1022) is offset from the pacing signal (1000) by a time offset (1004) as indicated in FIG. 10. The time offset (1004) can be smaller than about 25 milliseconds, in some embodiments. At the next heartbeat, a similarly defined common refractory time window (1052) is the next time window available for application of the ablation waveform(s). In this manner, the ablation waveform(s) may be applied over a series of heartbeats, at each heartbeat remaining within the common refractory time window. In one embodiment, each packet of pulses as defined above in the pulse waveform hierarchy can be applied over a heartbeat, so that a series of packets is applied over a series of heartbeats, for a given electrode set.

[0173] As used herein, the terms “about” and/or “approximately” when used in conjunction with numerical values and/or ranges generally refer to those numerical values and/or ranges near to a recited numerical value and/or range. In some instances, the terms “about” and “approximately” may mean within $\pm 10\%$ of the recited value. For example, in some instances, “about 100 [units]” may mean within $\pm 10\%$ of 100 (e.g., from 90 to 110). The terms “about” and “approximately” may be used interchangeably.

[0174] Some embodiments described herein relate to a computer storage product with a non-transitory computer-readable medium (also may be referred to as a non-transitory processor-readable medium) having instructions or computer code thereon for performing various computer-implemented operations. The computer-readable medium (or processor-readable medium) is non-transitory in the sense that it does not include transitory propagating signals per se (e.g., a propagating electromagnetic wave carrying information on a transmission medium such as space or a cable). The media and computer code (also may be referred to as code or algorithm) may be those designed and constructed for the specific purpose or purposes. Examples of non-transitory computer-readable media include, but are not limited to, magnetic storage media such as hard disks, floppy disks, and magnetic tape; optical storage media such as Compact Disc/Digital Video Discs (CD/DVDs), Compact Disc-Read Only Memories (CD-ROMs), and holographic devices; magneto-optical storage media such as optical disks; carrier wave signal processing modules; and hardware devices that are specially configured to store and execute program code, such as Application-Specific Integrated Circuits (ASICs), Programmable Logic Devices (PLDs), Read-Only Memory (ROM) and Random-Access Memory (RAM)

devices. Other embodiments described herein relate to a computer program product, which may include, for example, the instructions and/or computer code disclosed herein.

[0175] The systems, devices, and/or methods described herein may be performed by software (executed on hardware), hardware, or a combination thereof. Hardware modules may include, for example, a general-purpose processor (or microprocessor or microcontroller), a field programmable gate array (FPGA), and/or an application specific integrated circuit (ASIC). Software modules (executed on hardware) may be expressed in a variety of software languages (e.g., computer code), including C, C++, Java®, Ruby, Visual Basic®, and/or other object-oriented, procedural, or other programming language and development tools. Examples of computer code include, but are not limited to, micro-code or micro-instructions, machine instructions, such as produced by a compiler, code used to produce a web service, and files containing higher-level instructions that are executed by a computer using an interpreter. Additional examples of computer code include, but are not limited to, control signals, encrypted code, and compressed code.

[0176] The specific examples and descriptions herein are exemplary in nature and embodiments may be developed by those skilled in the art based on the material taught herein without departing from the scope of the present invention, which is limited only by the attached claims.

CLAIMS

We Claim:

1. An apparatus, comprising:

a catheter shaft defining a longitudinal axis;

an inflatable member coupled to a distal end of the catheter shaft;

a first set of electrodes formed on a surface of the catheter shaft; and

a second electrode formed on the inflatable member and electrically isolated from the first set of electrodes.

2. An apparatus, comprising:

a catheter shaft defining a longitudinal axis;

an inflatable member coupled to a distal end of the catheter shaft;

a first set of electrodes formed on the inflatable member and disposed proximal to an equatorial plane of the inflatable member; and

a second set of electrodes formed on the inflatable member and disposed distal to the equatorial plane of the inflatable member, the second set of electrodes being electrically isolated from the first set of electrodes.

3. An apparatus, comprising:

a catheter shaft defining a longitudinal axis;

an inflatable member coupled to a distal end of the catheter shaft, the inflatable member having an outer surface including a set of electrically conductive portions;

a first set of electrodes formed on a surface of the catheter shaft; and

a second set of electrodes formed distal to the first set of electrodes on the surface of the catheter shaft, the second set of electrodes electrically coupled to the outer surface of the inflatable member and electrically isolated from the first set of electrodes.

4. A system, comprising:

a signal generator configured for generating a pulse waveform;

an ablation device coupled to the signal generator and configured for receiving the pulse waveform, the ablation device including:

a handle;

a catheter shaft defining a longitudinal axis;

an inflatable member coupled to a distal end of the catheter shaft,

a first set of electrodes formed on a surface of the catheter shaft; and

a second set of electrodes formed on the outer surface of the inflatable member and electrically isolated from the first set of electrodes.

5. An apparatus, comprising:

a catheter shaft defining a longitudinal axis;

an annular inflatable member coupled to a distal end of the catheter shaft, the inflatable member defining an annular inflatable member lumen therethrough;

a first electrode disposed on a distal end of the annular inflatable member, the first electrode having a substantially planar portion; and

a second electrode extending from, and distal to, the annular inflatable member lumen and spaced apart from the first electrode.

6. The apparatus of claim 1, further including a second set of electrodes formed on the inflatable member between the first set of electrodes and the second electrode.

7. The apparatus of claim 6, wherein the second electrode is independently addressable.
8. The apparatus of claim 6, wherein each electrode of the second set of electrodes is independently addressable.
9. The apparatus of claims 1 or 6, wherein the second set of electrodes are formed on the inflatable member on an approximate plane approximately perpendicular to the longitudinal axis.
10. The apparatus of claim 1 or 6, wherein each electrode of the second set of electrodes has a circular or elliptical shape.
11. The apparatus of claim 10, wherein a major axis of each electrode of the second set of electrodes having the elliptical shape is substantially parallel to the longitudinal axis.
12. The apparatus as in claims 2 and 3, the first set of electrodes having a polarity opposite to a polarity of the second set of electrodes during delivery of a pulse waveform.
13. The apparatus of claim 1, the first set of electrodes having a polarity opposite to the polarity of the second electrode during delivery of a pulse waveform.
14. The apparatus of claim 4, the first set of electrodes having a polarity opposite to the polarity of the second set of electrodes during delivery of the pulse waveform.
15. The apparatus as in claims 1, 3, and 4, wherein the catheter shaft includes a deflectable portion formed between the first set of electrodes and the second set of electrodes, the deflectable portion configured for deflecting a portion of the catheter including the second set of electrodes and the inflatable member up to about 210 degrees relative to the longitudinal axis.
16. The apparatus as in claims 1, 3, and 4, further comprising a fluid source coupled to the inflatable member and configured to inflate the inflatable member.
17. The apparatus as in claims 2-4, wherein one or more electrodes of the first set of electrodes and one or more electrodes of the second set of electrodes has an insulated electrical

lead associated therewith, the insulated electrical lead configured for sustaining a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation, the insulated electrical lead disposed in a lumen of the catheter shaft.

18. The apparatus of claim 1, wherein one or more electrodes of the first set of electrodes and the second electrode has an insulated electrical lead associated therewith, the insulated electrical lead configured for sustaining a voltage potential of at least about 700 V without dielectric breakdown of its corresponding insulation, the insulated electrical lead disposed in a lumen of the catheter shaft.

19. The apparatus as in claims 2-4, wherein one or more electrodes of the first set of electrodes and one or more electrodes of the second set of electrodes are independently addressable.

20. The apparatus of claim 1, wherein one or more electrodes of the first set of electrodes and the second electrode are independently addressable.

21. The apparatus as in claims 1, 3, and 4, wherein a distal-most electrode of the first set of electrodes is spaced apart from a proximal most electrode of the second set of electrodes by between about 4 mm and about 10 mm.

22. The apparatus as in claims 1, 3, and 4, wherein a distal-most electrode of the first set of electrodes is spaced apart by at least about 5 mm from a proximal end of the inflatable member.

23. The apparatus as in claims 3 and 4, wherein the first set of electrodes are formed on a portion of the catheter shaft having a length of between about 3 mm and about 12 mm.

24. The apparatus as in claims 1, 3, and 4, wherein the inflatable member has a cross-sectional diameter in its equatorial plane of between about 5 mm and about 15 mm.

25. The apparatus as in claims 1, 3, and 4, wherein the inflatable member has a length of up to about 22 mm.

26. The apparatus as in claims 1, 3, and 4, wherein each electrode of the first set of electrodes has a width of between about 1 mm and about 5 mm and wherein adjacent electrodes of the first set of electrodes are spaced apart by between about 1 mm and about 5 mm.

27. The apparatus as in claims 1, 3, and 4, wherein the inflatable member has an asymmetric shape in a proximal-to-distal direction.

28. The apparatus as in claims 1, 3, and 4, wherein the inflatable member has a bulbous shape.

29. The apparatus as in claims 1, 3, and 4, wherein the inflatable member has a polyhedral shape.

30. The apparatus as in claims 1, 3, and 4, further including a biocompatible coating formed on an outer surface of the inflatable member.

31. The apparatus as in claims 1, 3, and 4, wherein the distal end of the catheter extends into an inner volume of the inflatable member.

32. The apparatus as in claims 1, 3, and 4, further including a set of splines coupled to the catheter and an inner surface of the inflatable member, the set of splines configured for translation along the longitudinal axis to transition between:

a first configuration wherein the set of splines are approximately parallel to the longitudinal axis; and

a second configuration wherein the set of splines bias away from the longitudinal axis.

33. The system of claim 4, the pulse waveform including:

a first level of a hierarchy of the pulse waveform includes a first set of pulses, each pulse having a pulse time duration, a first time interval separating successive pulses;

a second level of the hierarchy of the pulse waveform includes a plurality of first sets of pulses as a second set of pulses, a second time interval separating successive first sets of pulses, the second time interval being at least three times the duration of the first time interval; and

a third level of the hierarchy of the pulse waveform includes a plurality of second sets of pulses as a third set of pulses, a third time interval separating successive second sets of pulses, the third time interval being at least thirty times the duration of the second level time interval.

34. The system of claim 33, wherein the pulse waveform includes a fourth level of the hierarchy of the pulse waveform includes a plurality of third sets of pulses as a fourth set of pulses, a fourth time interval separating successive third sets of pulses, the fourth time interval being at least ten times the duration of the third level time interval.

35. The apparatus as in claims 1-5, wherein a distal portion of the catheter shaft further includes a radiopaque portion.

36. The apparatus as in claims 1-5, wherein the catheter shaft defines a shaft lumen therethrough.

37. The apparatus as in claims 1, 3, and 4, wherein the first set of electrodes are formed on a distal portion of the catheter shaft.

38. The apparatus as in claim 3, wherein there are no electrodes formed on the outer surface of the inflatable member.

39. The apparatus as in claim 1, further including a conductive element formed on a surface of the inflatable member.

40. The apparatus of claim 39, wherein the conductive element includes a set of spaced apart conductive stripes extending between ends of the inflatable member.

41. The apparatus of claim 39, wherein the conductive element is electrically connected to the second set of electrodes.

42. The apparatus of claim 39, wherein each stripe of the set of stripes intersect at one or more of a proximal end and a distal end of the inflatable member.

43. The apparatus of claim 39, wherein the conductive element includes an interlaced structure defining a set of apertures.

44. The apparatus as in claims 1 and 2, further including a first conductive element disposed on an outer surface of the inflatable member and a second conductive element disposed on an inner surface of the inflatable member, wherein the first conductive element has an opposite polarity to the second conductive element during delivery of a pulse waveform.

45. The apparatus of claim 1, wherein the second electrode is configured to receive electrophysiology data.

46. The apparatus of claim 1, wherein the second electrode is a distal electrode.

47. The apparatus as in claim 1, wherein the second electrode is the only electrode formed on the outer surface of the inflatable member.

48. The apparatus as in claim 1, wherein a distal end of the inflatable member has a concave surface facing away from a proximal end of the inflatable member.

49. The apparatus of claim 29, wherein the inflatable member has a set of curved faces.

50. The apparatus of claim 49, wherein at least one electrode of the second set of electrodes is formed on one face of the inflatable member.

51. The apparatus of claim 50, wherein one or more electrodes of the second set of electrodes are concave.

52. The apparatus of claim 49, wherein the inflatable member has a set of curved edges.

53. The apparatus of claim 29, wherein each electrode of the second set of electrodes has a diameter of between about 3 mm and about 15 mm.

54. The apparatus of claim 29, wherein a distal-most electrode of the first set of electrodes is spaced apart from a proximal end of the inflatable member by at least about 3 mm.

55. The apparatus of claim 29, wherein the inflatable member in the second configuration has a cross-sectional diameter at its largest portion of between about 6 mm and about 22 mm.

56. The apparatus of claim 5, wherein the annular inflatable member in the second configuration has a diameter of between about 10 mm and about 15 mm.

57. The apparatus of claim 5, wherein the second electrode has a length of between about 8 mm and about 10 mm.

58. The apparatus of claim 5, wherein the annular inflatable member lumen has a diameter of between about 4 mm and about 15 mm.

59. The apparatus of claims 1 or 2, wherein the second set of electrodes includes a distal electrode formed at a distal end of the inflatable member.

60. The apparatus of claim 59, wherein each electrode of the second set of electrodes has a circular or elliptical shape.

61. The apparatus of claim 60, wherein a major axis of each electrode of the second set of electrodes having the elliptical shape except the distal electrode is substantially parallel to the longitudinal axis.

62. A method of focal ablation via irreversible electroporation, comprising:

advancing an ablation device towards an endocardial wall, the ablation device including:

a catheter shaft defining a longitudinal axis;

an inflatable member coupled to a distal end of the catheter shaft;

a first set of electrodes formed on a surface of the catheter shaft; and

a second set of electrodes formed on the outer surface of the inflatable member and electrically isolated from the first set of electrodes;

generating a pulse waveform; and

delivering the pulse waveform to the endocardial wall via the ablation device.

63. The method of claim 62, further comprising:

configuring one of the first set of electrodes and the second set of electrodes as anodes;

configuring the other of the first set of electrodes and the second set of electrodes as cathodes.

64. The method of claim 62, further comprising:

transitioning the inflatable member of the ablation device from a first configuration to a second configuration.

65. The method of claim 64, wherein transitioning the inflatable member from the first configuration to the second configuration includes infusing the inflatable member with saline.

66. The method of claim 62, further comprising:

delivering pulsed electric field ablation energy through the first set of electrodes and the second set of electrodes of the ablation device.

67. The method of claim 62, wherein the ablation device is configured to generate an electric field intensity in tissue of between about 200 V/cm and about 800 V/cm.

68. The method of claim 62, the ablation device including a handle, the method further comprising:

deflecting a portion of the ablation device using the handle.

69. The method of claim 62, further comprising:

recording first electrophysiology data of the endocardial wall;

recording second electrophysiology data of the endocardial wall after delivering the pulse waveform.

70. The method of claim 69, wherein the first electrophysiology data and the second electrophysiology data includes intracardiac ECG signal data of the endocardial wall.

71. The method of claim 69, further comprising advancing a diagnostic catheter into the endocardial wall and recording the first electrophysiology data and the second electrophysiology data using the diagnostic catheter.

72. The method of claim 69, wherein the first electrophysiology data and the second electrophysiology data is recorded using the ablation device in the second configuration.

73. The method of claim 62, further comprising:
creating a transseptal opening into a left atrium;
advancing a guidewire and a sheath into the left atrium through the transseptal opening;
and
advancing the ablation device into a ventricle over the guidewire.

74. The method of claim 72, further comprising:
creating a first access site in a patient;
advancing the guidewire through the first access site and into a right atrium;
advancing the dilator and a sheath over the guidewire and into the right atrium;
advancing the dilator from the right atrium into the left atrium through an interatrial septum to create the transseptal opening; and
dilating the transseptal opening using the dilator.

75. The method of claim 74, further comprising:
advancing the cardiac stimulator into a ventricular chamber;
generating a pacing signal for cardiac stimulation of the heart using the cardiac stimulator; and

applying the pacing signal to the heart using the cardiac stimulator, the pulse waveform generated in synchronization with the pacing signal.

76. The method of claim 62, further comprising fluoroscopically imaging a radiopaque portion of the ablation device during one or more steps.

77. The method of claim 73, wherein the first access site is a femoral vein.

78. The method of claim 73, wherein the interatrial septum includes a fossa ovalis.

79. The method of claim 62, wherein the endocardial wall is a ventricle.

80. The method of claim 62, the pulse waveform including:

a first level of a hierarchy of the pulse waveform includes a first set of pulses, each pulse having a pulse time duration, a first time interval separating successive pulses;

a second level of the hierarchy of the pulse waveform includes a plurality of first sets of pulses as a second set of pulses, a second time interval separating successive first sets of pulses, the second time interval being at least three times the duration of the first time interval; and

a third level of the hierarchy of the pulse waveform includes a plurality of second sets of pulses as a third set of pulses, a third time interval separating successive second sets of pulses, the third time interval being at least thirty times the duration of the second level time interval.

81. The method of claim 80, wherein the pulse waveform includes a fourth level of the hierarchy of the pulse waveform includes a plurality of third sets of pulses as a fourth set of pulses, a fourth time interval separating successive third sets of pulses, the fourth time interval being at least ten times the duration of the third level time interval.

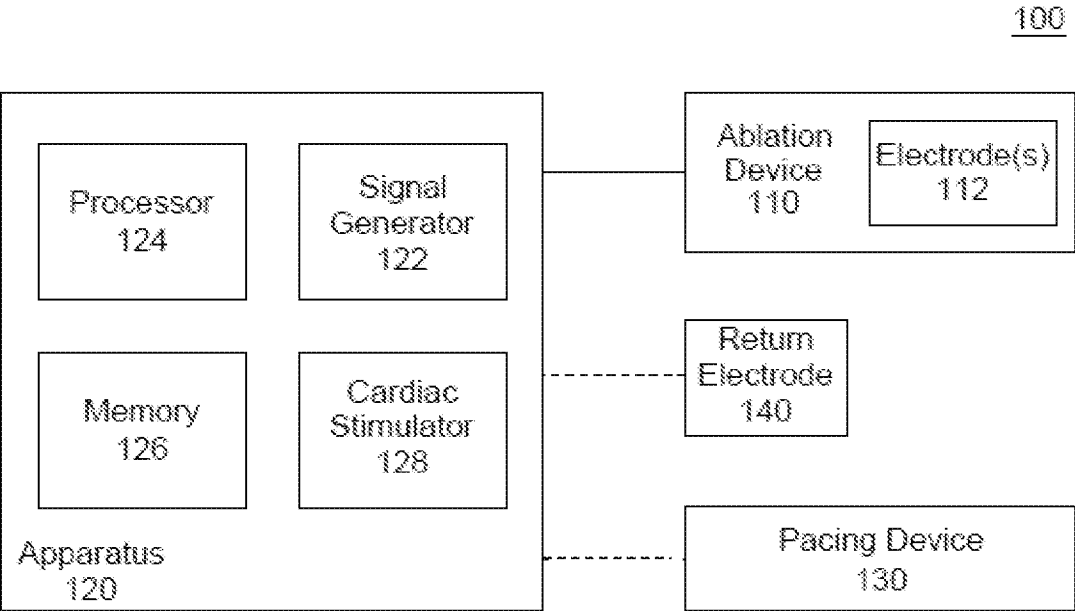


FIG. 1

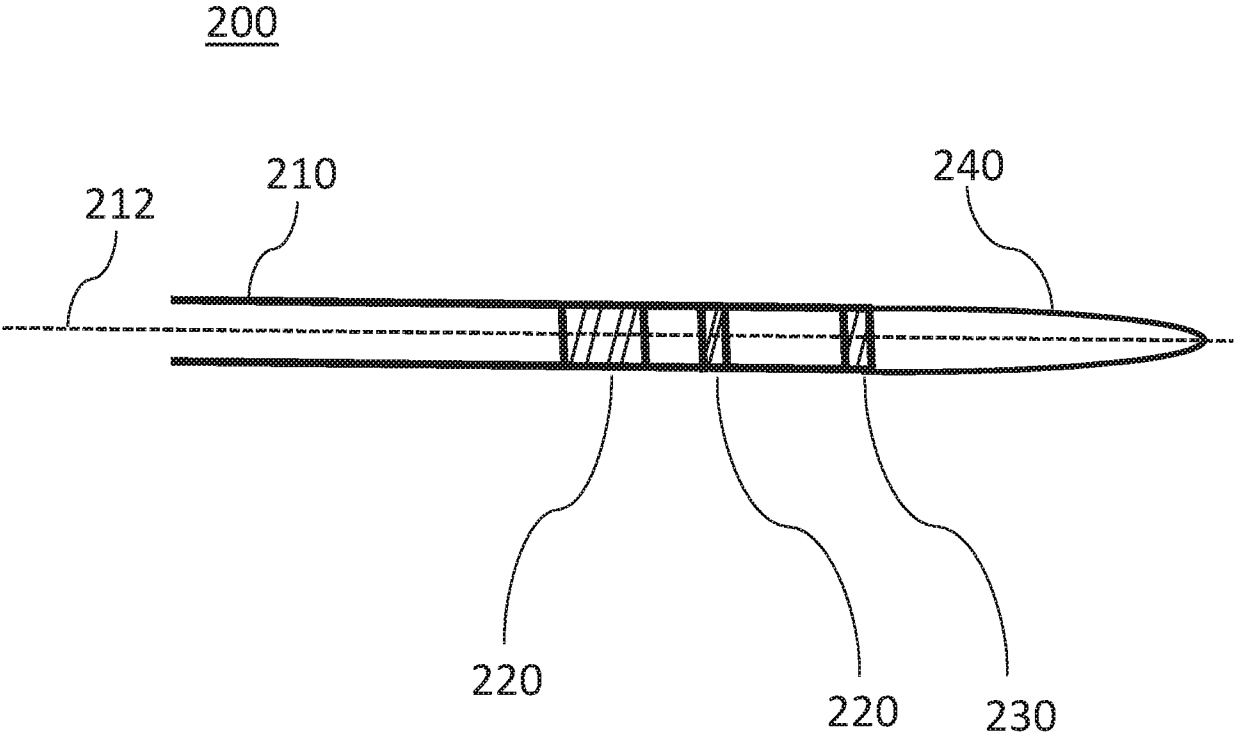


FIG. 2A

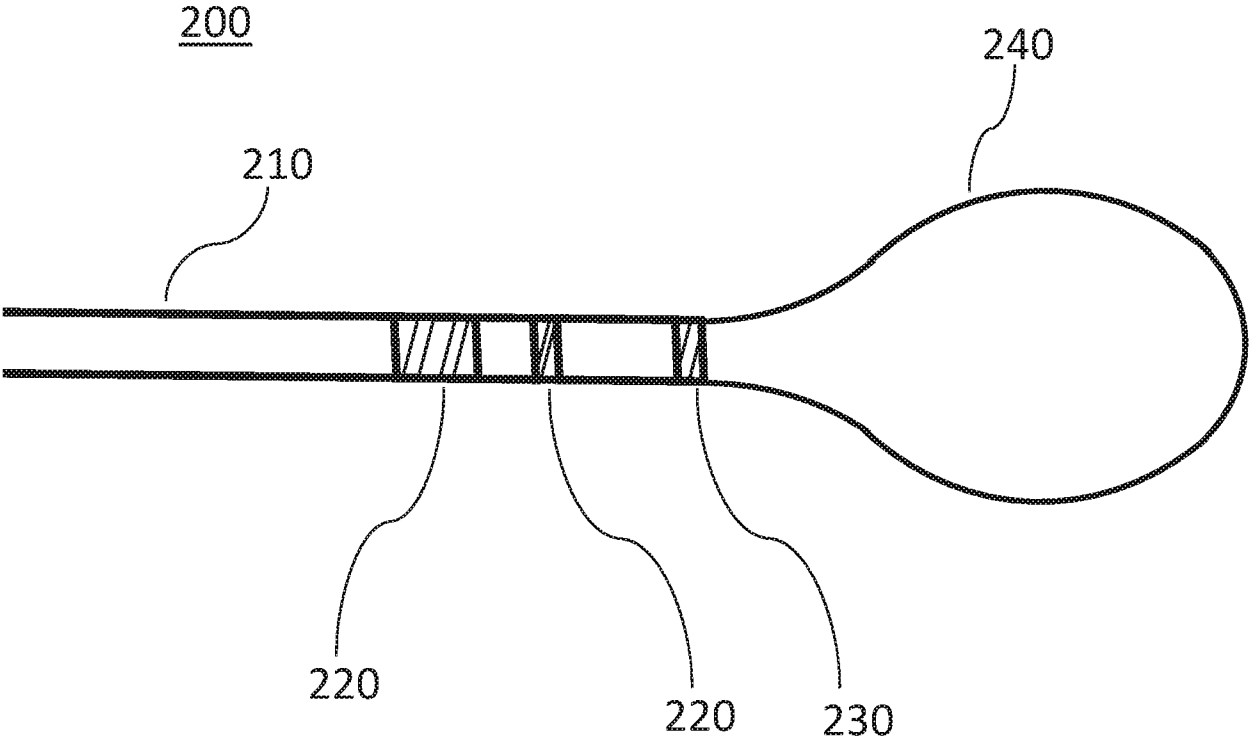


FIG. 2B

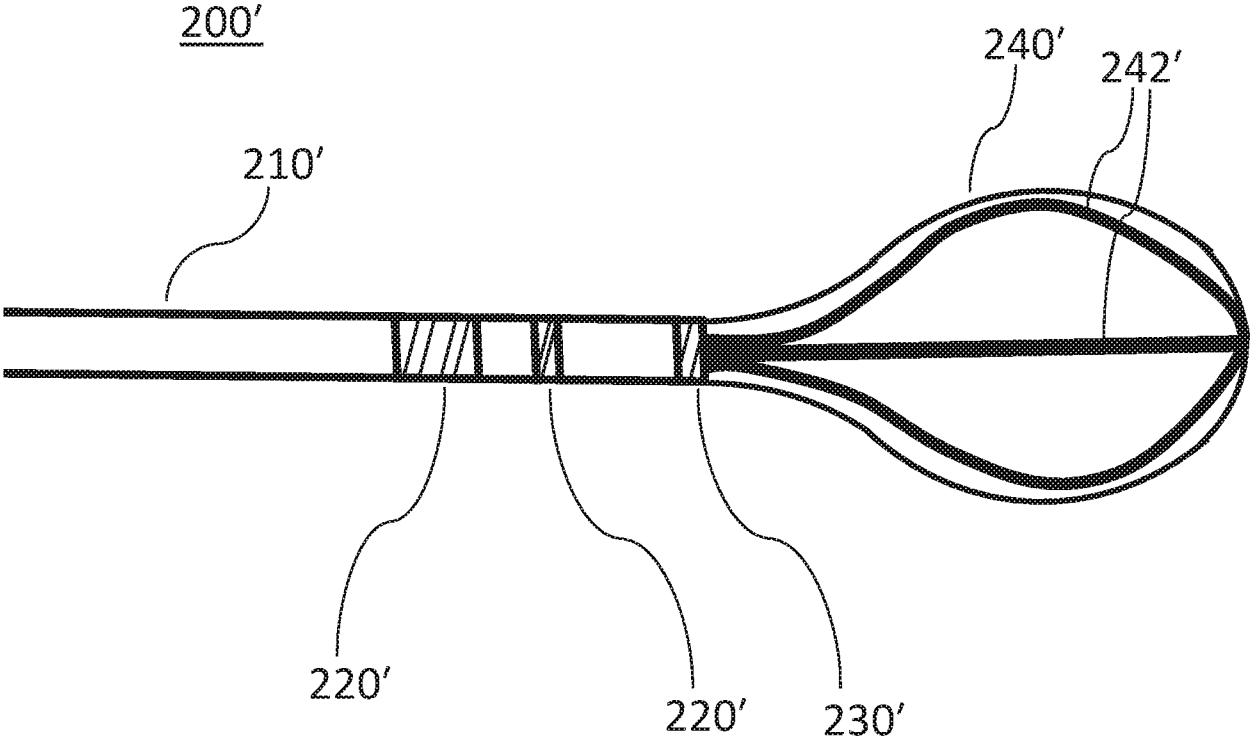


FIG. 2C

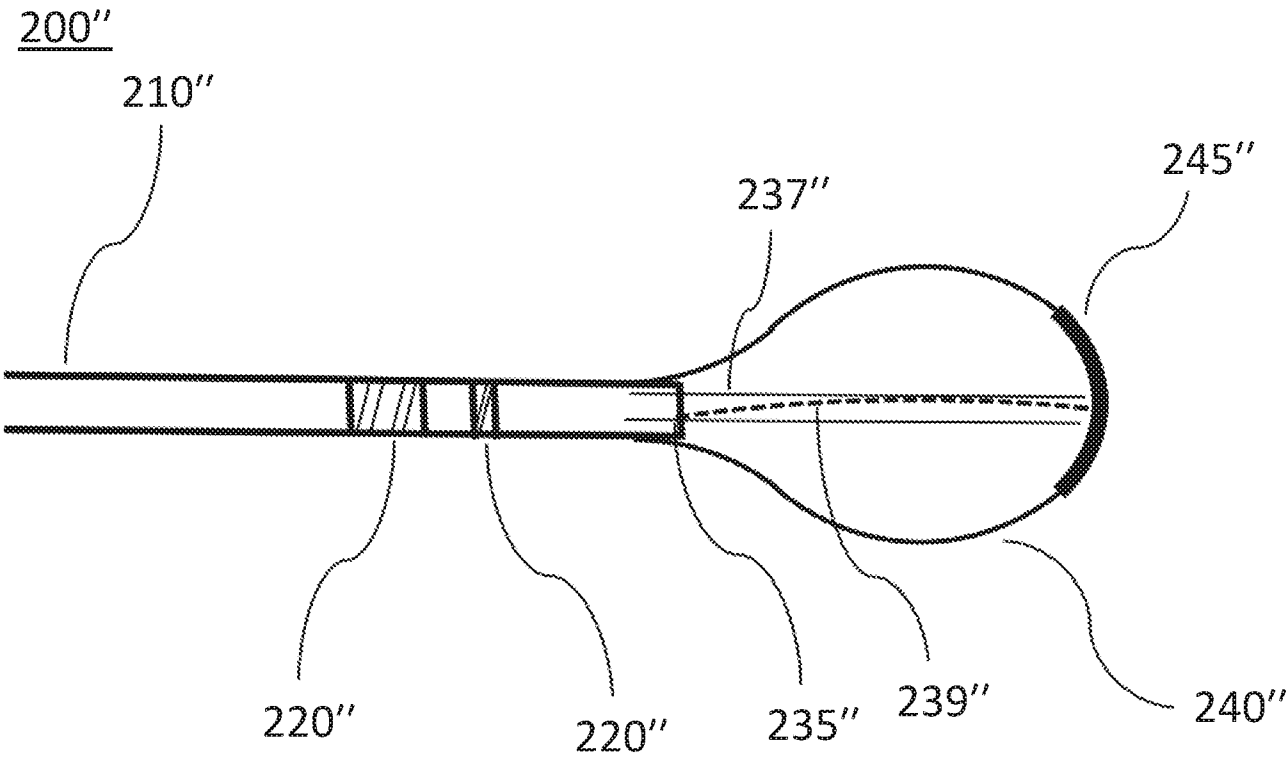


FIG. 2D

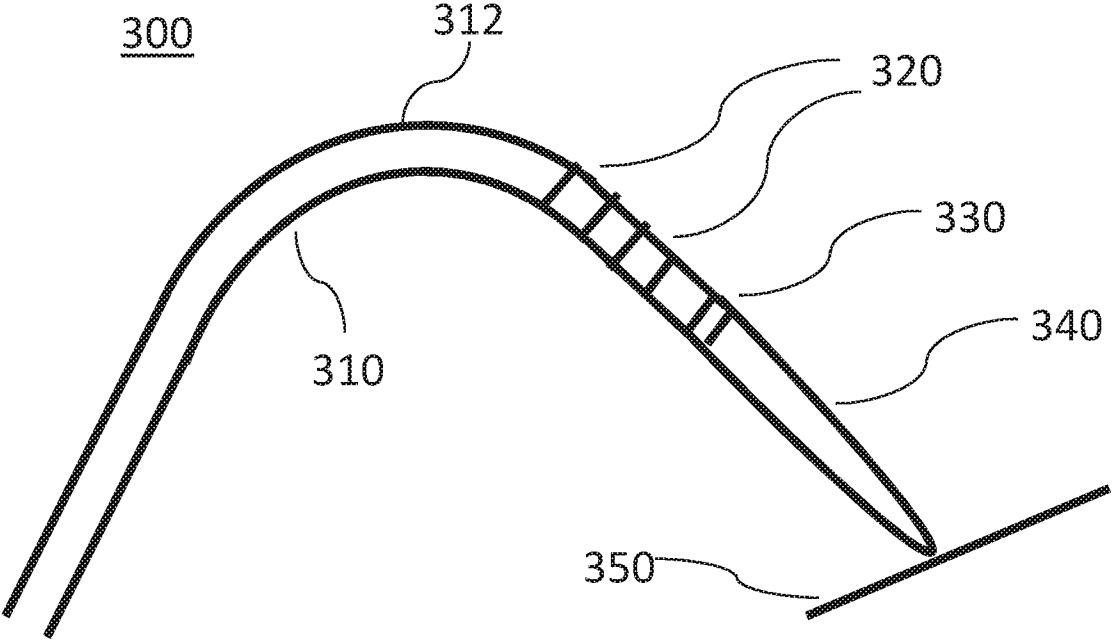


FIG. 3

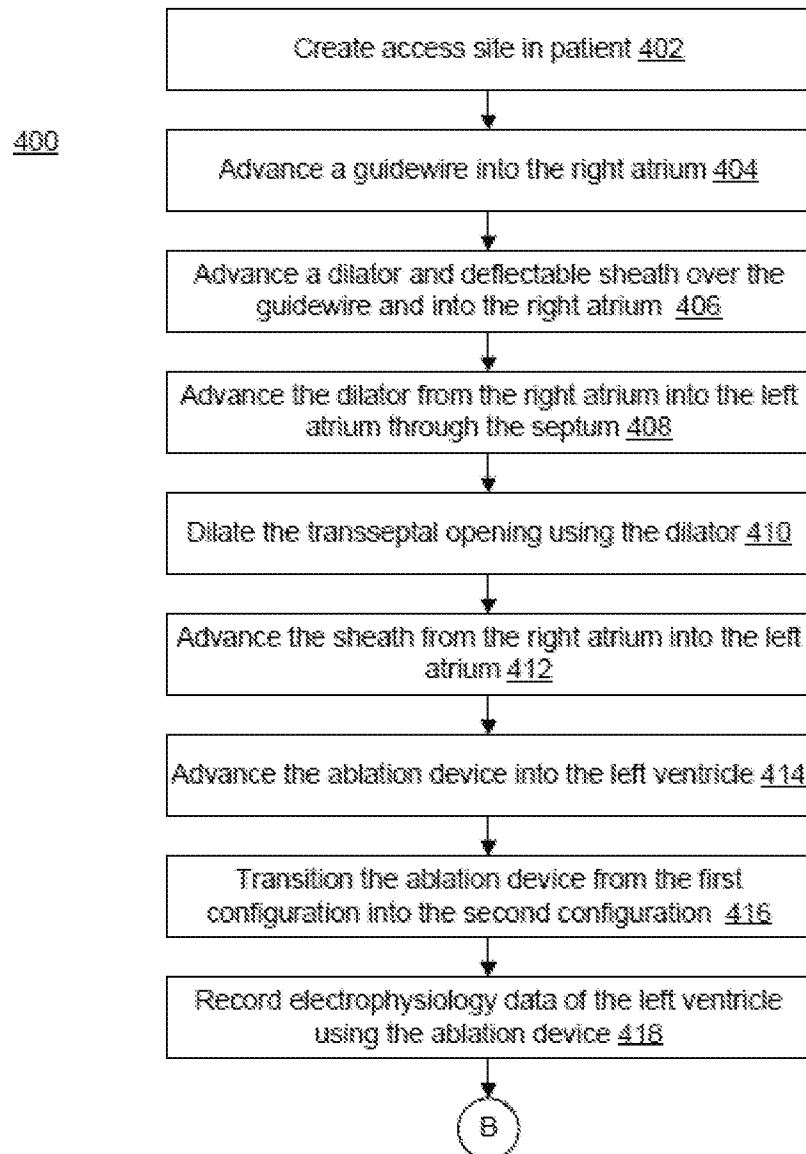


FIG. 4A

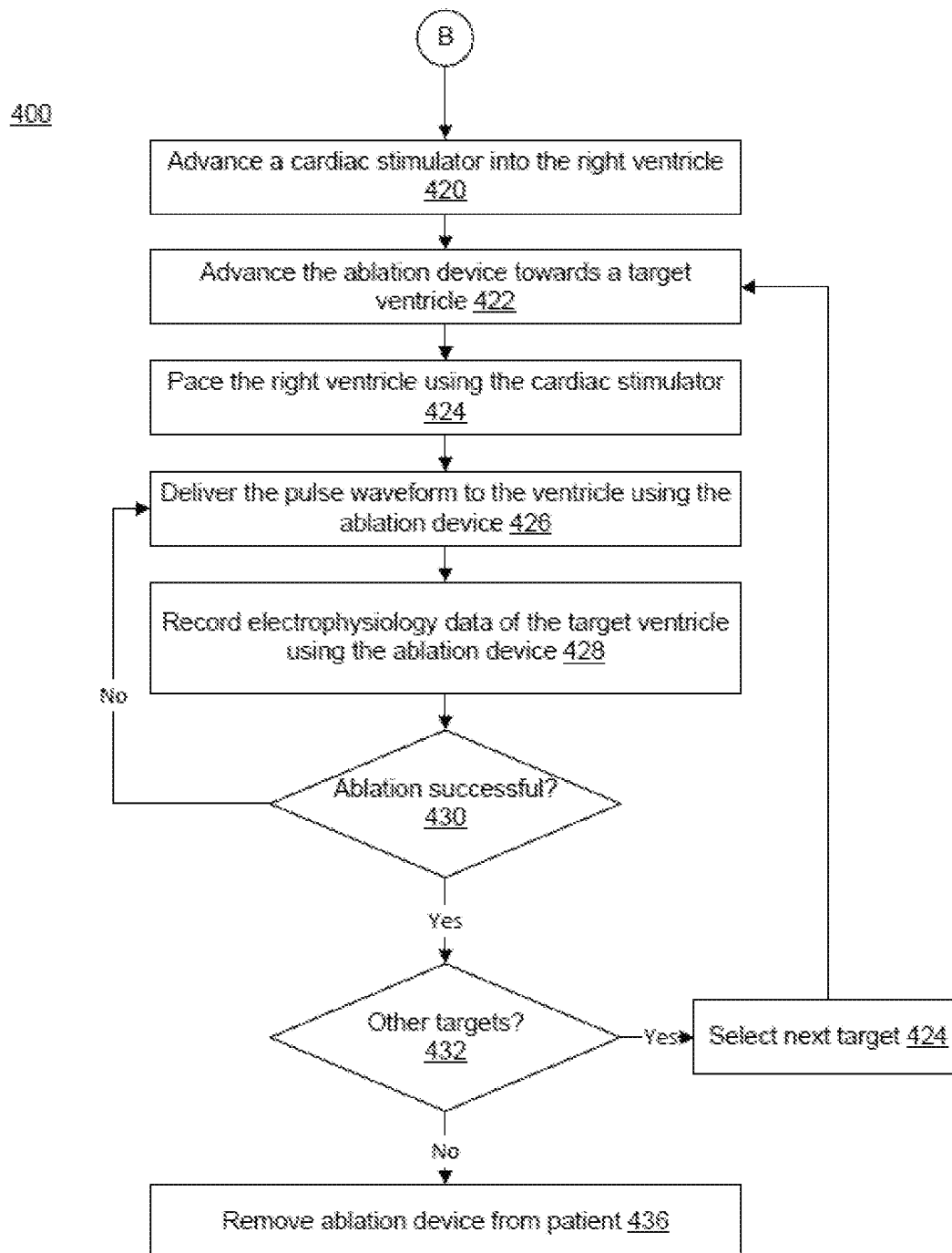


FIG. 4B

500

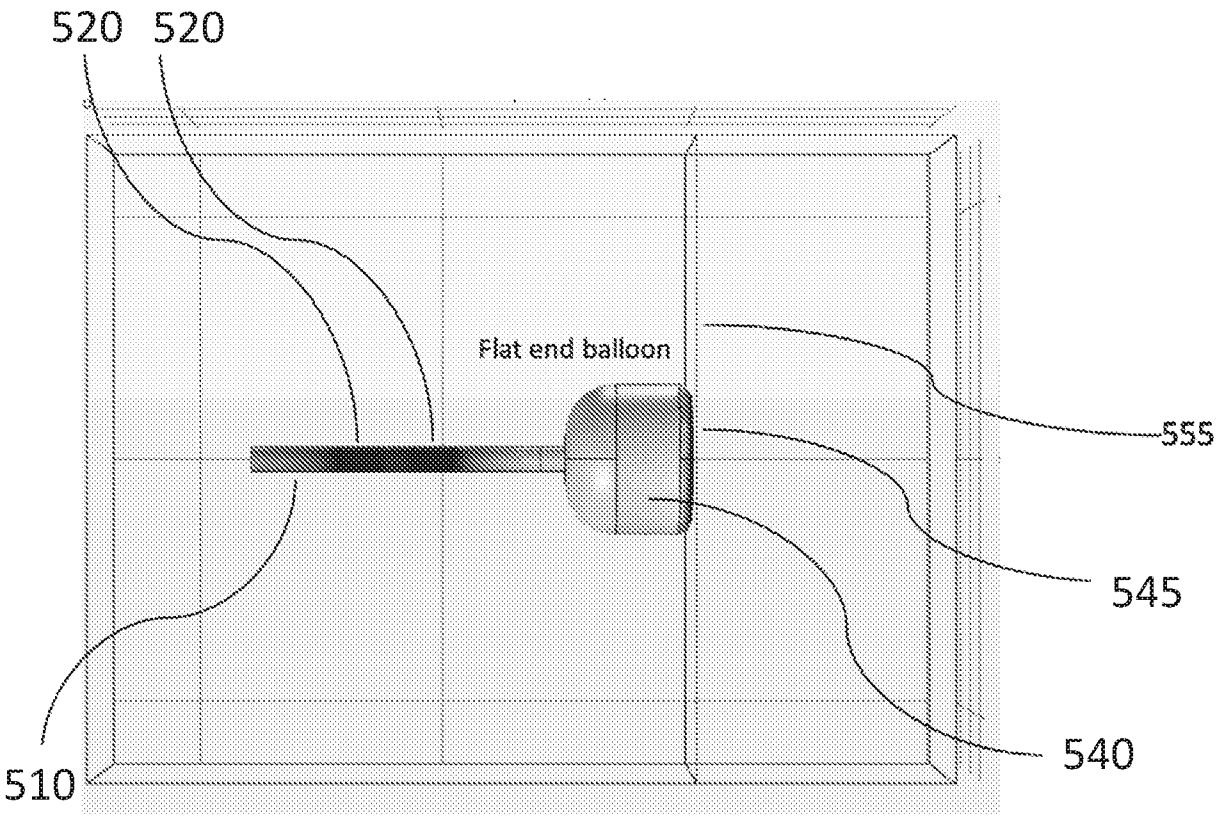


FIG. 5A

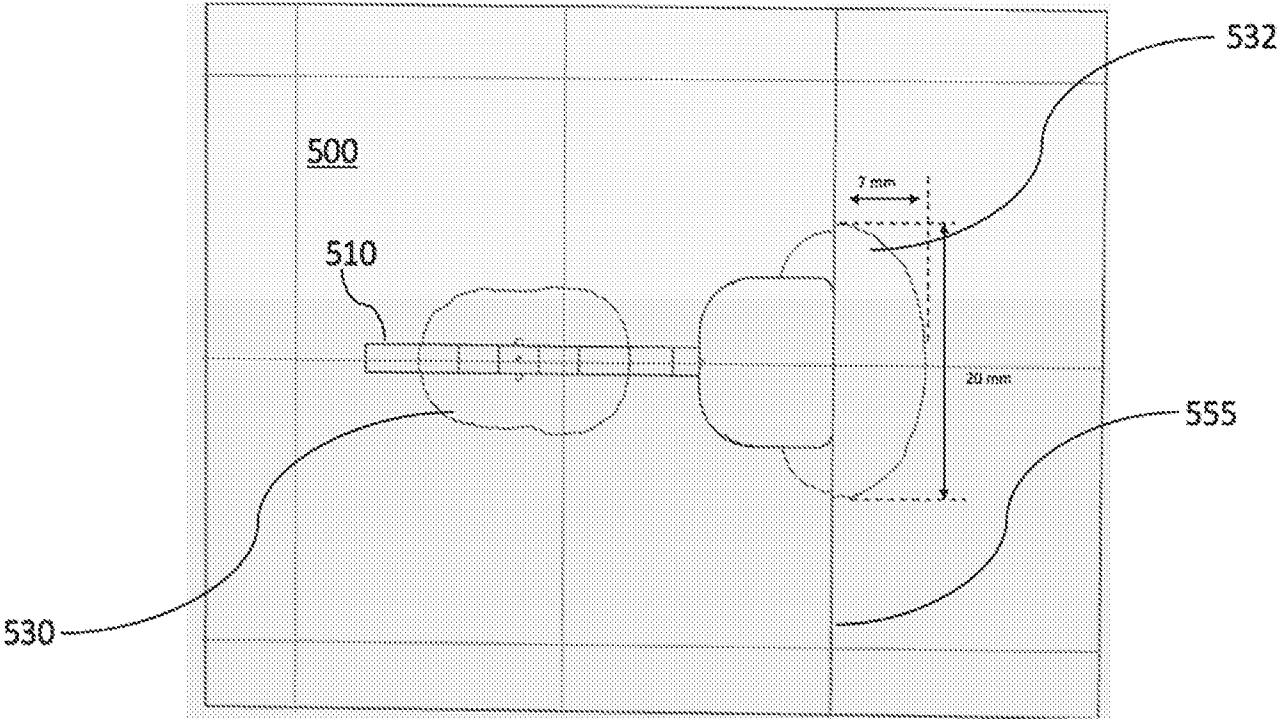


FIG. 5B

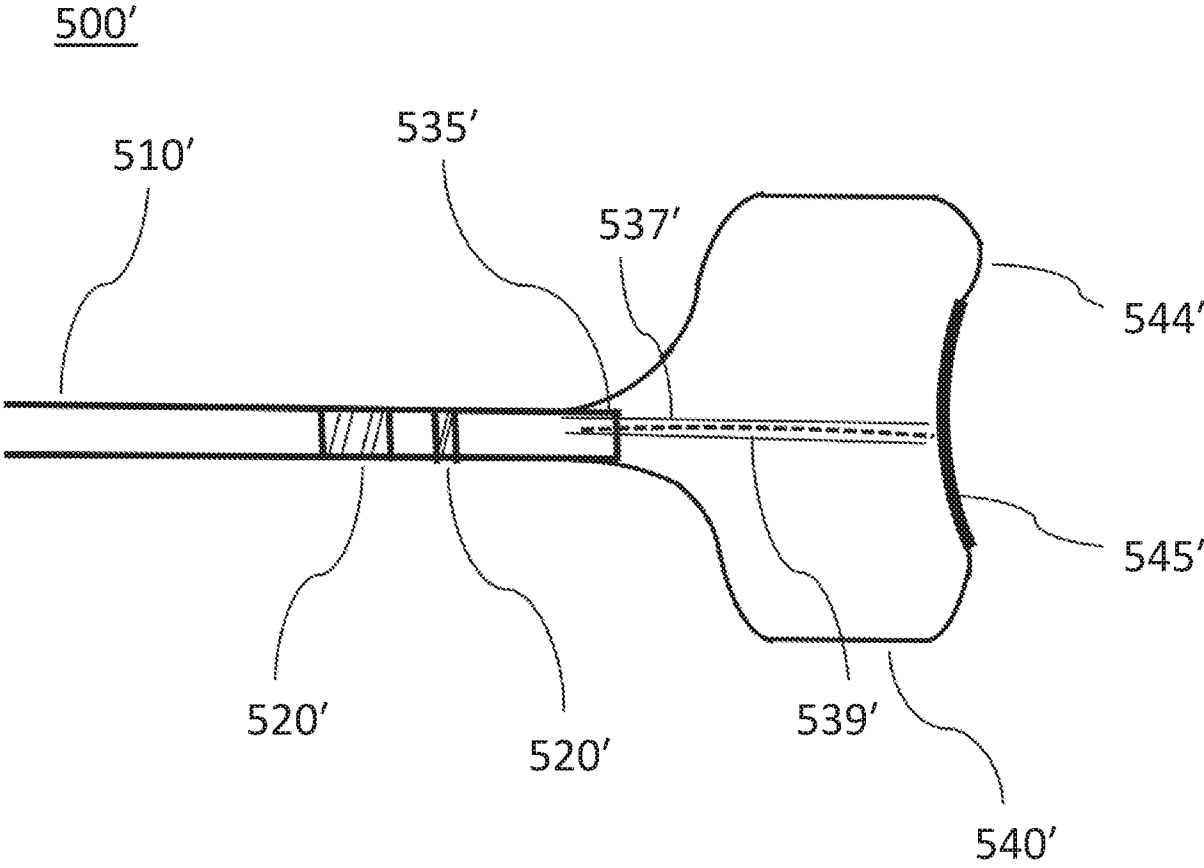


FIG. 5C

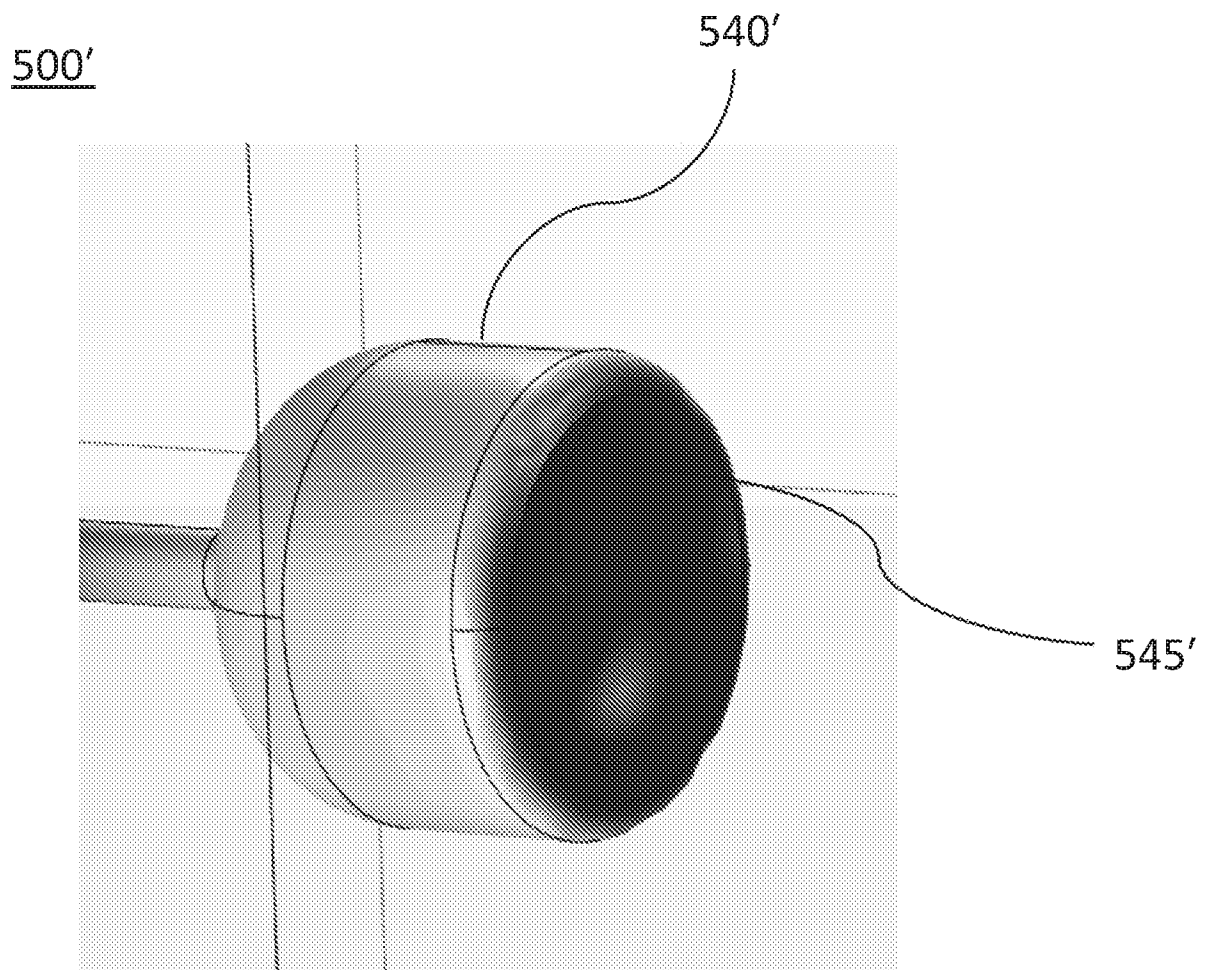


FIG. 5D

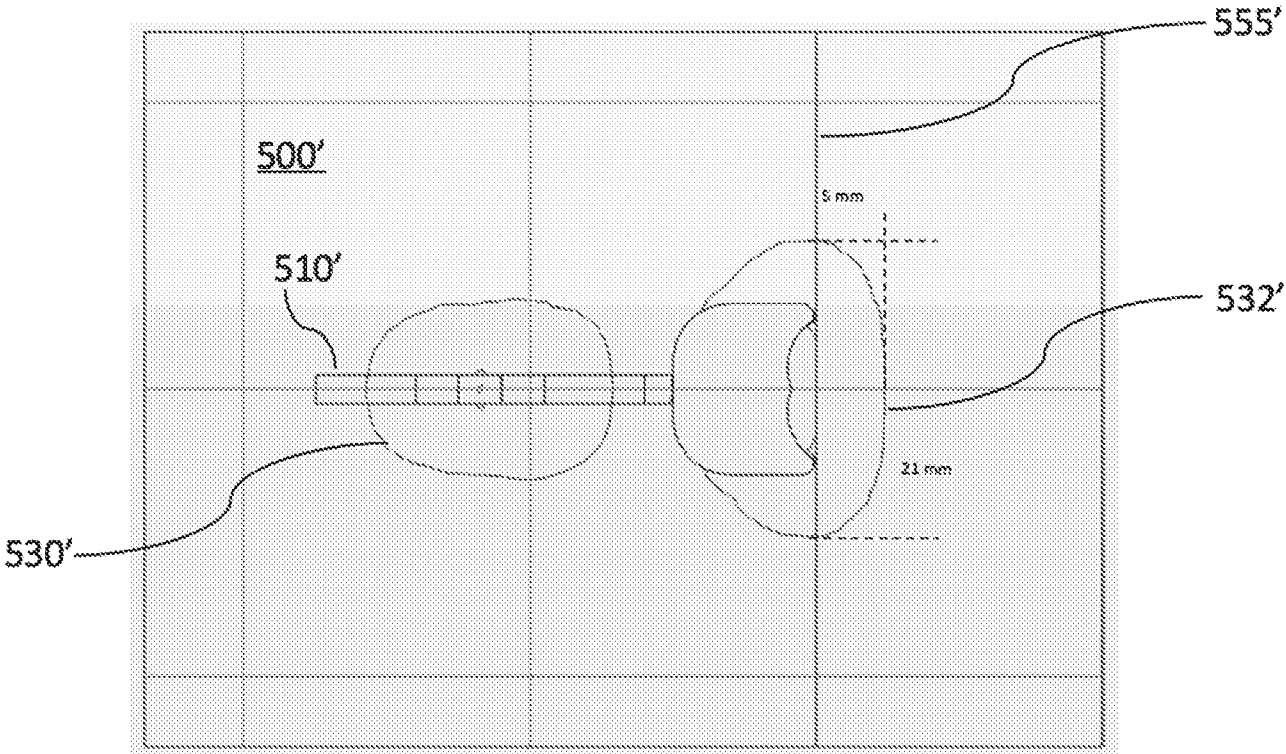


FIG. 5E

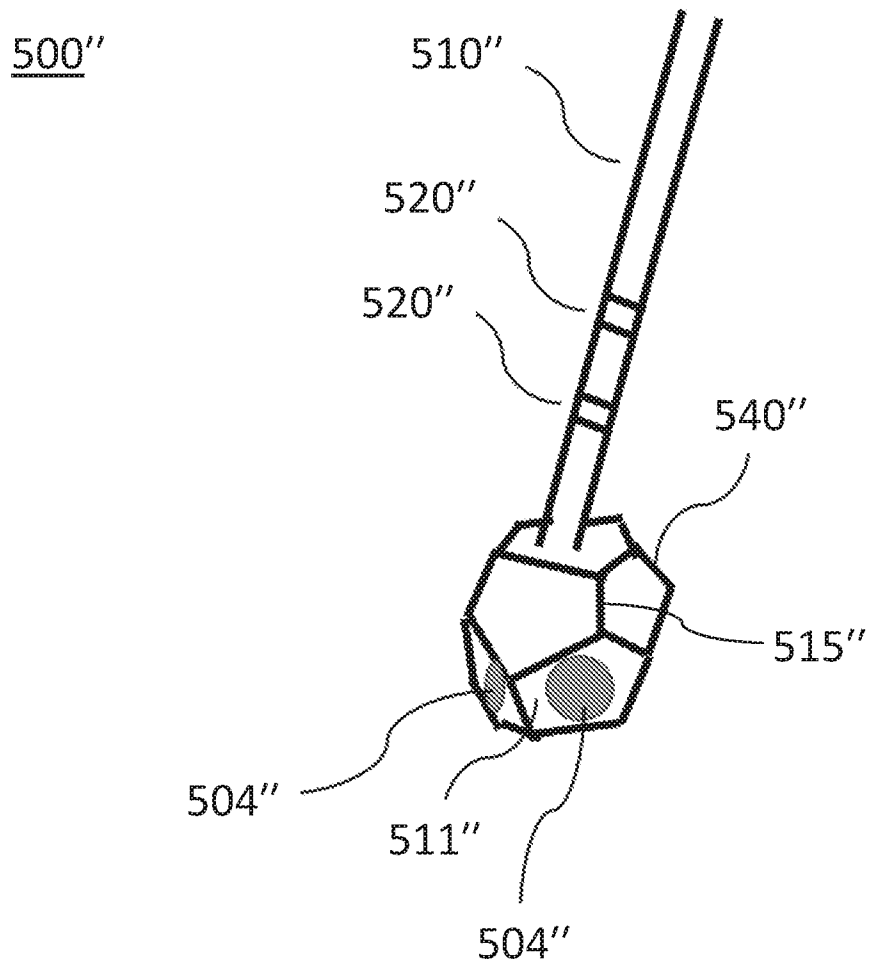


FIG. 5F

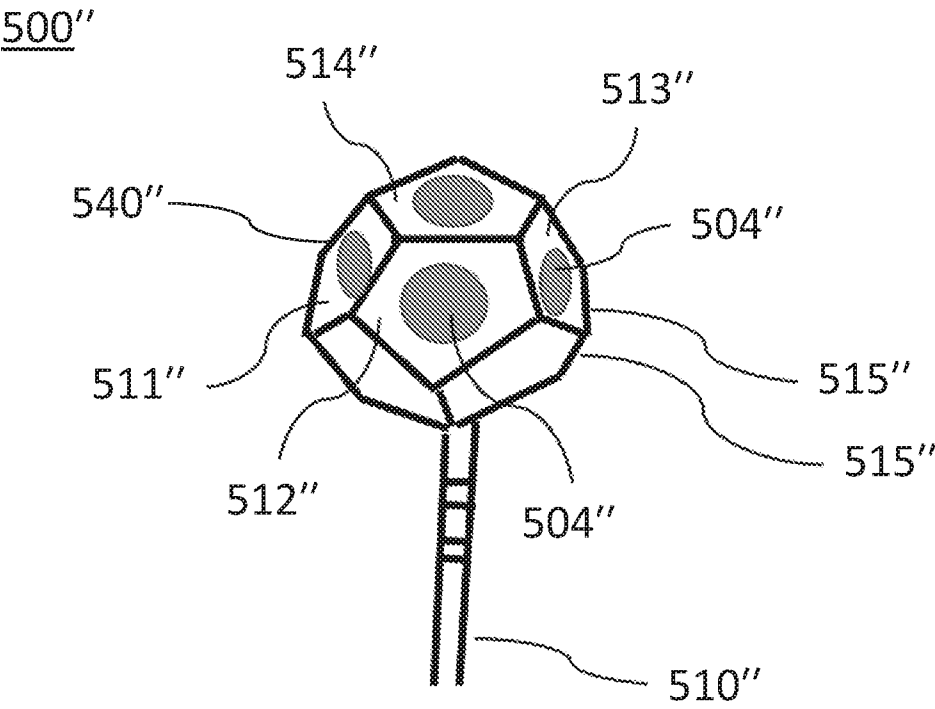


FIG. 5G

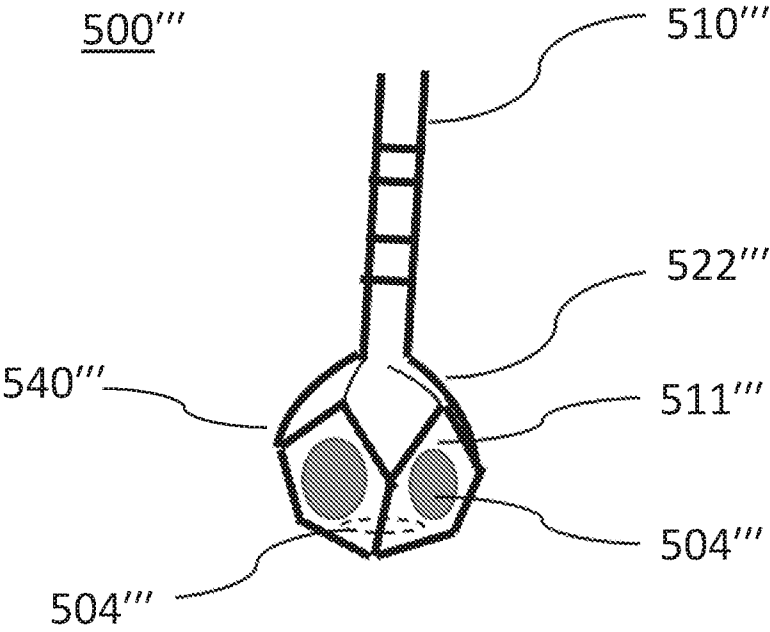


FIG. 5H

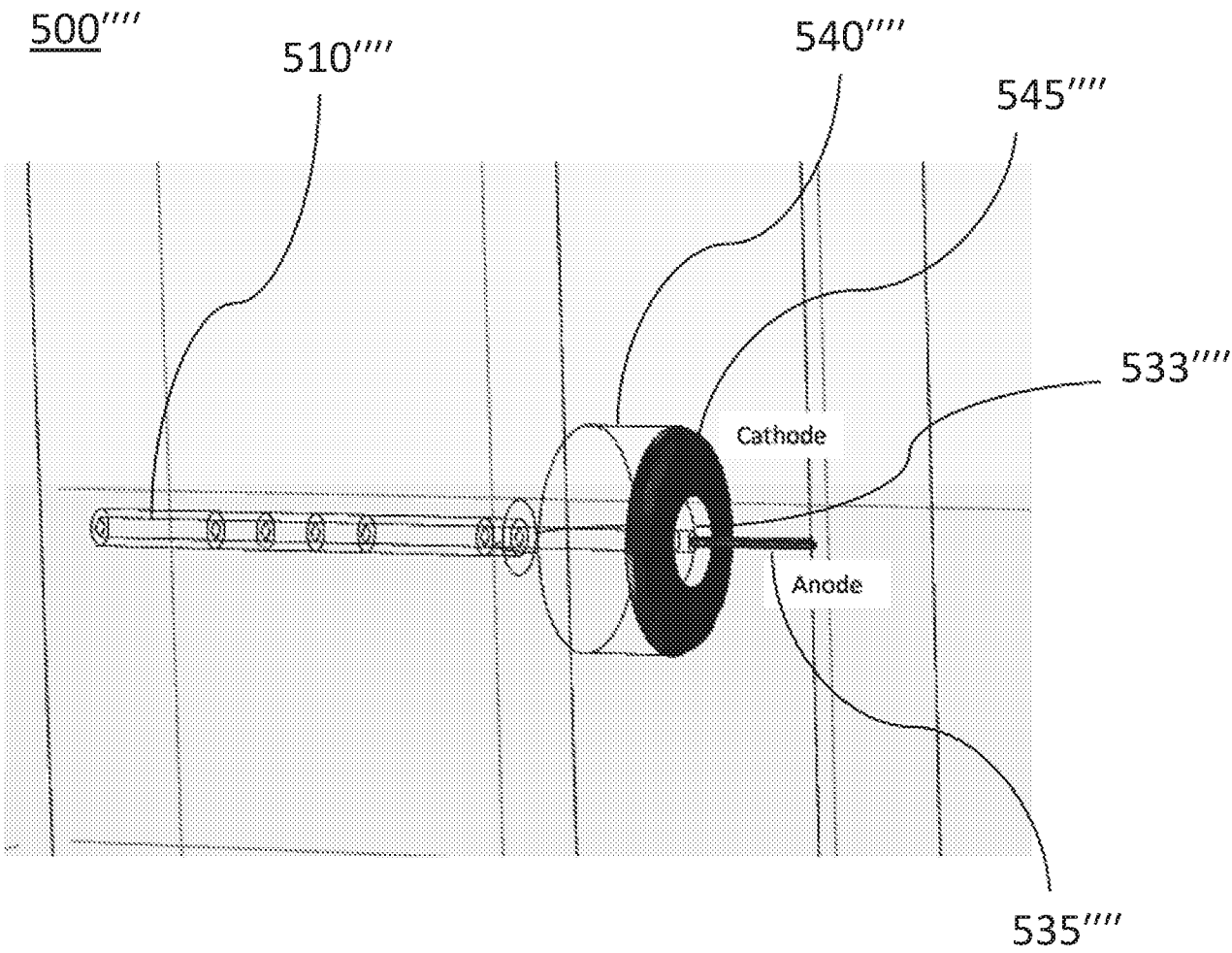


FIG. 5I

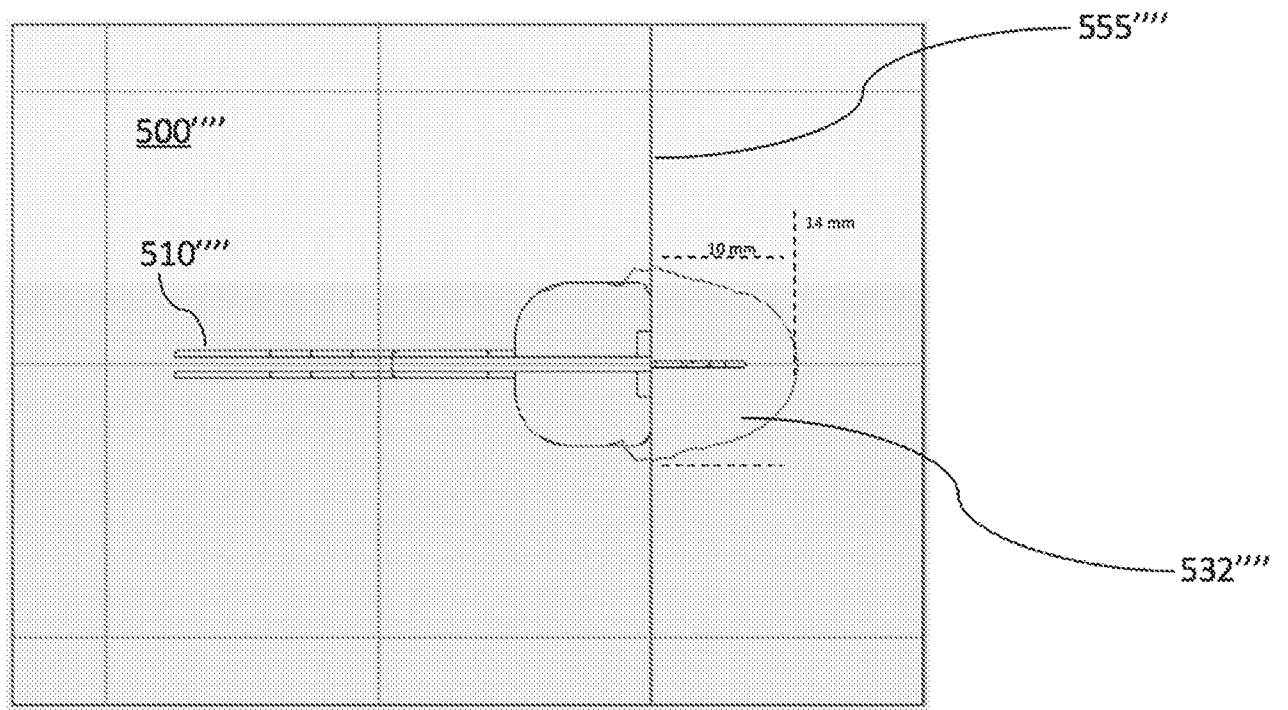


FIG. 5J

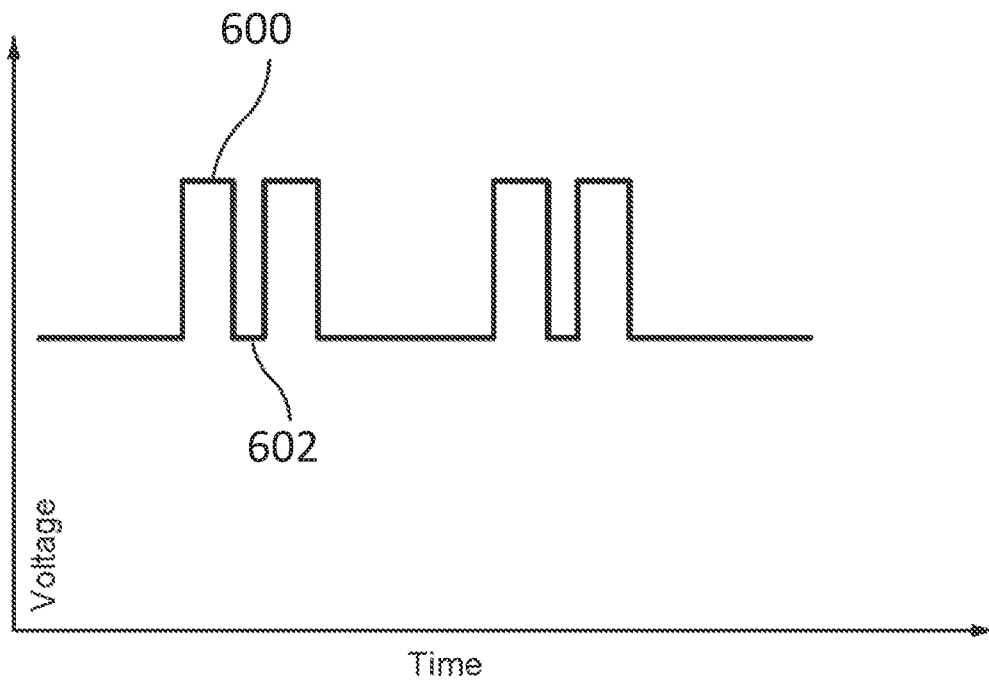


FIG. 6

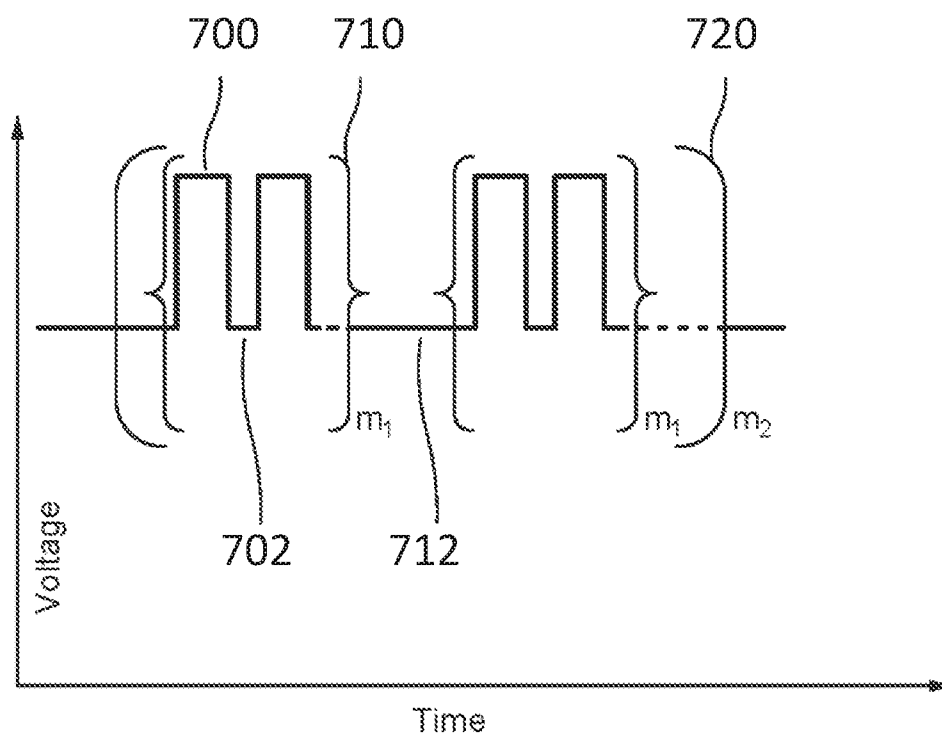


FIG. 7

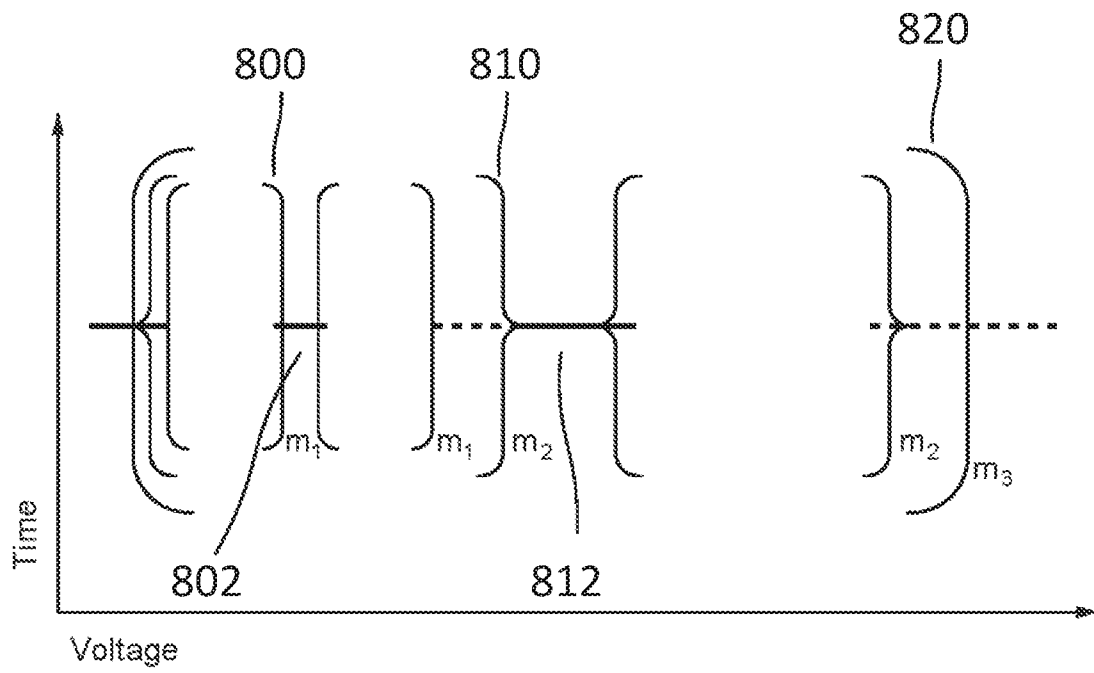


FIG. 8

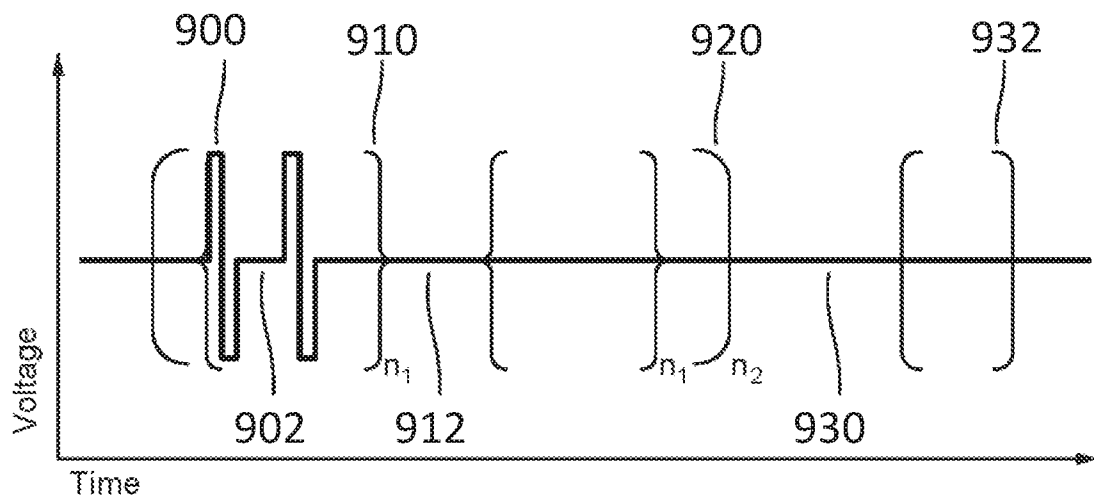


FIG. 9

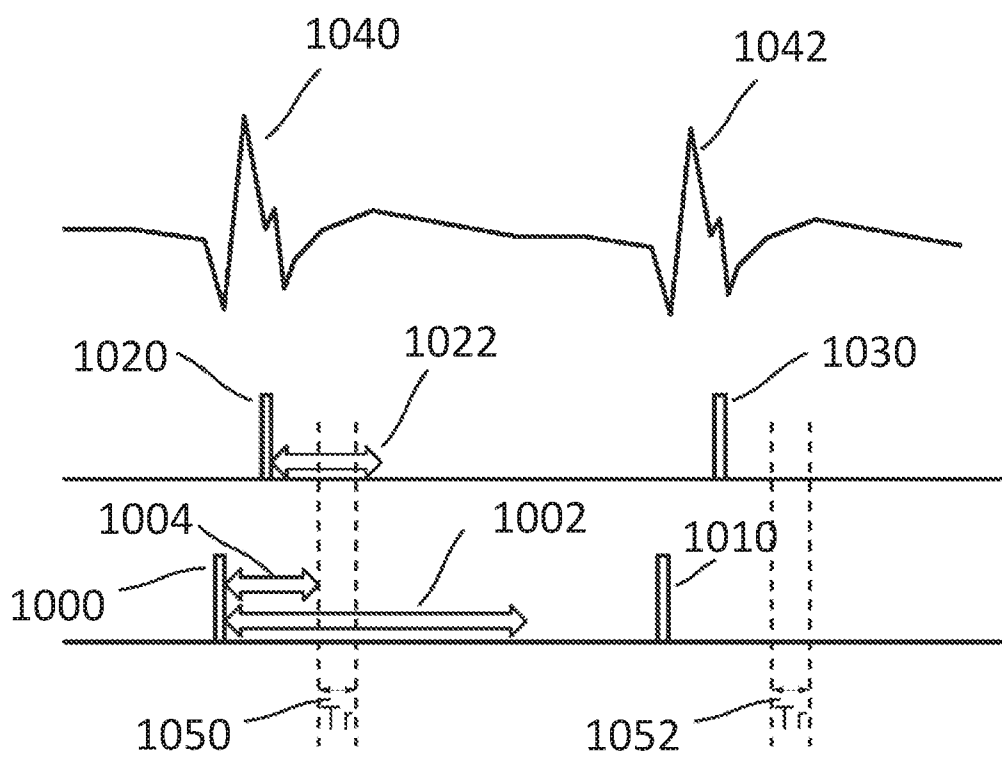


FIG. 10

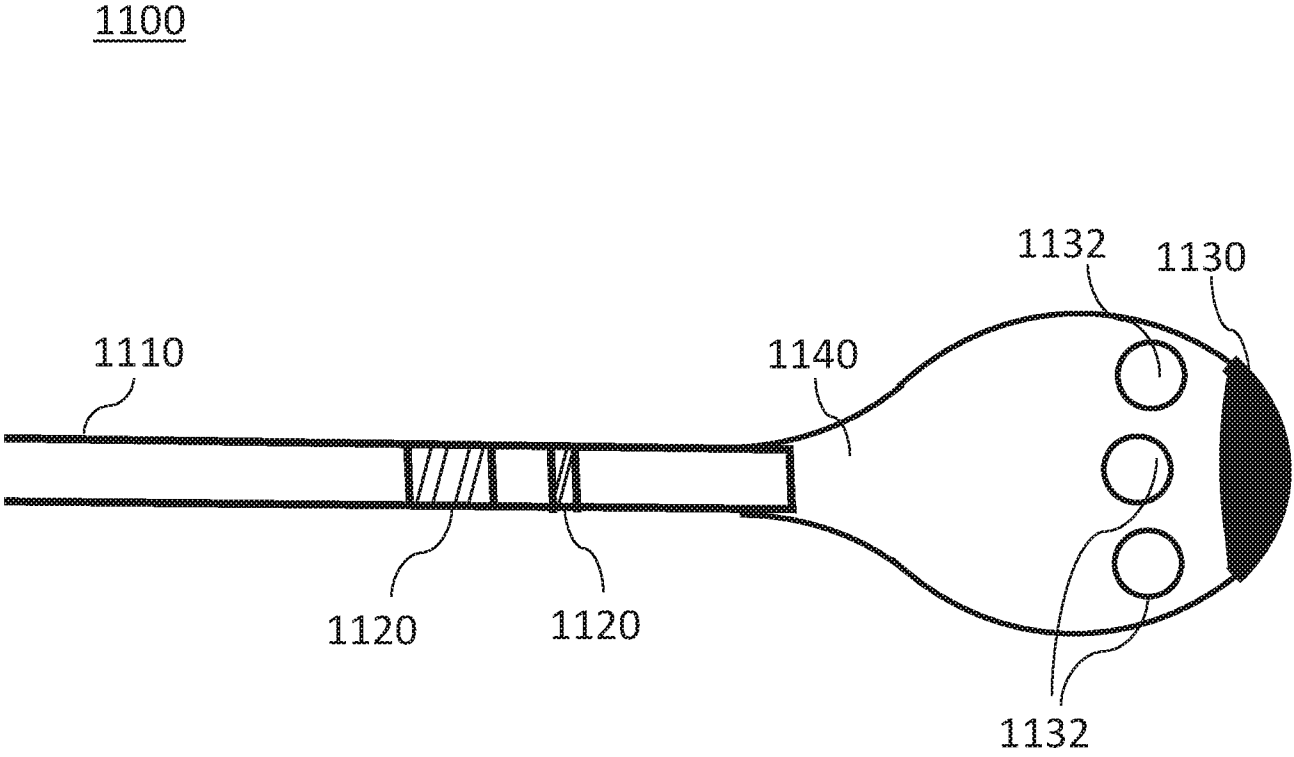


FIG. 11

1200

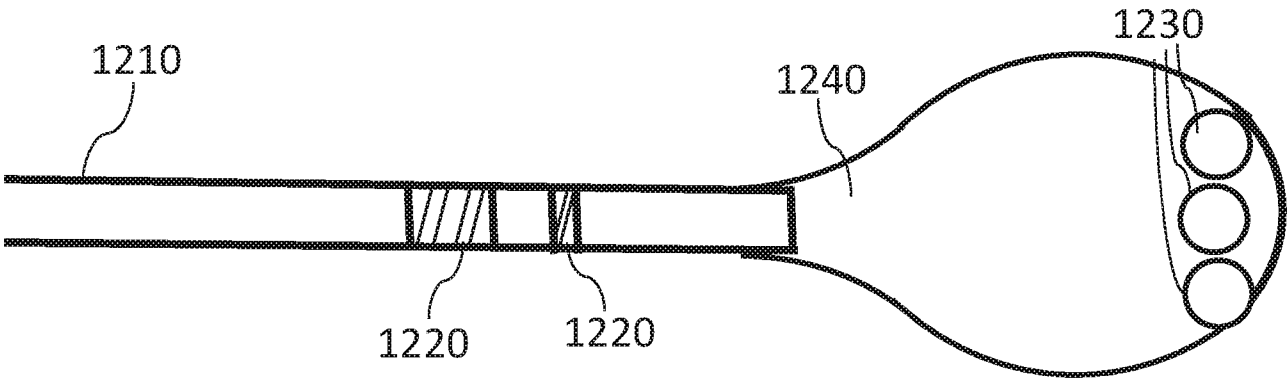


FIG. 12

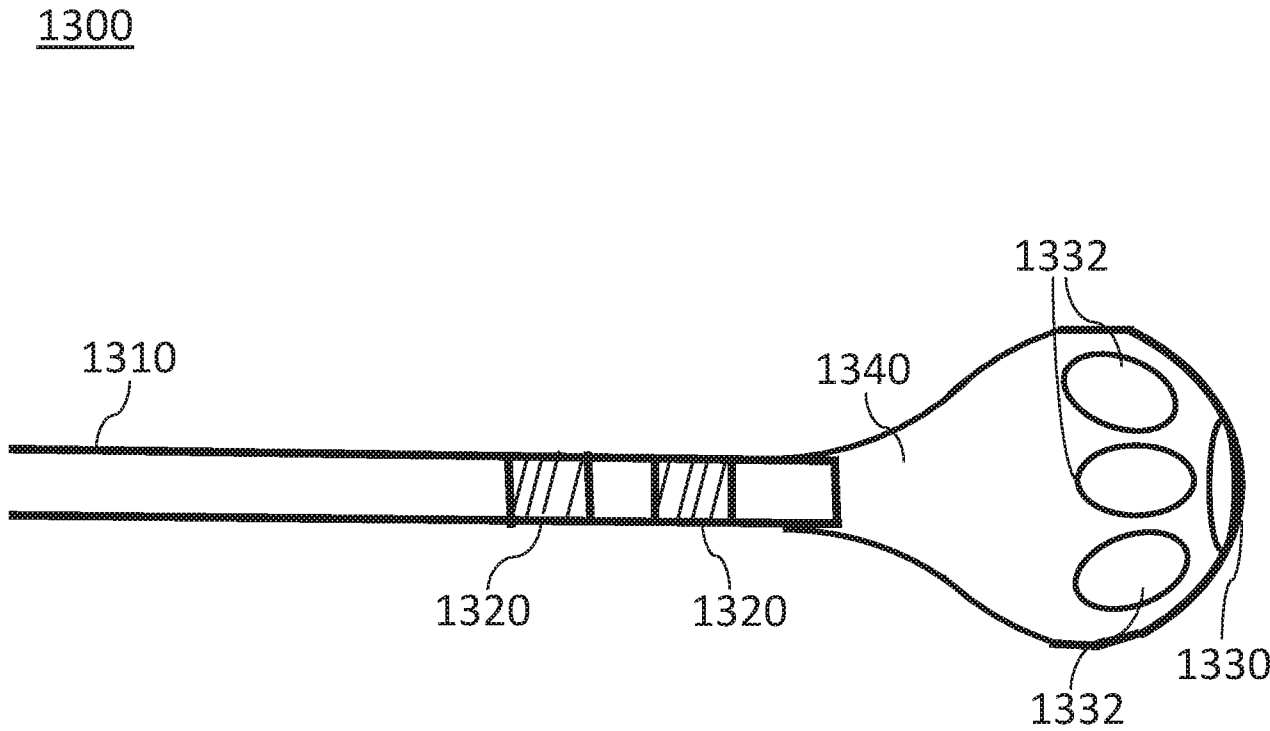


FIG. 13

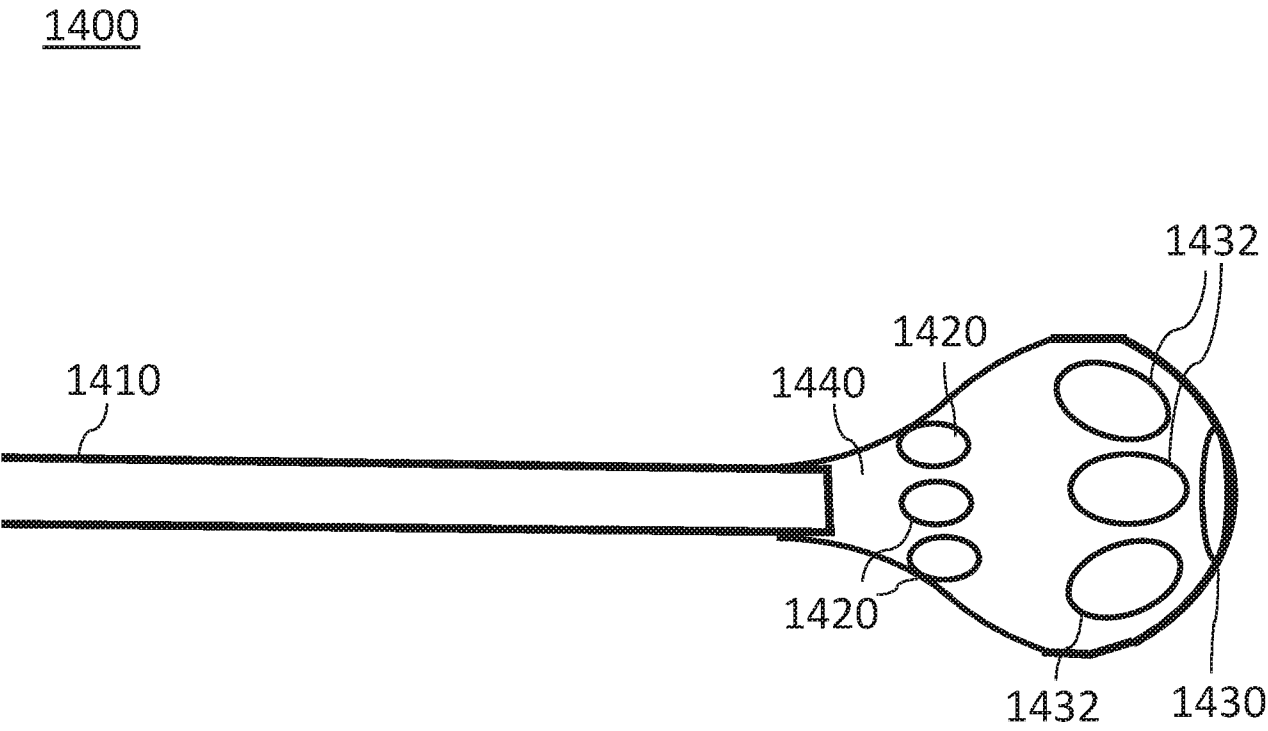


FIG. 14

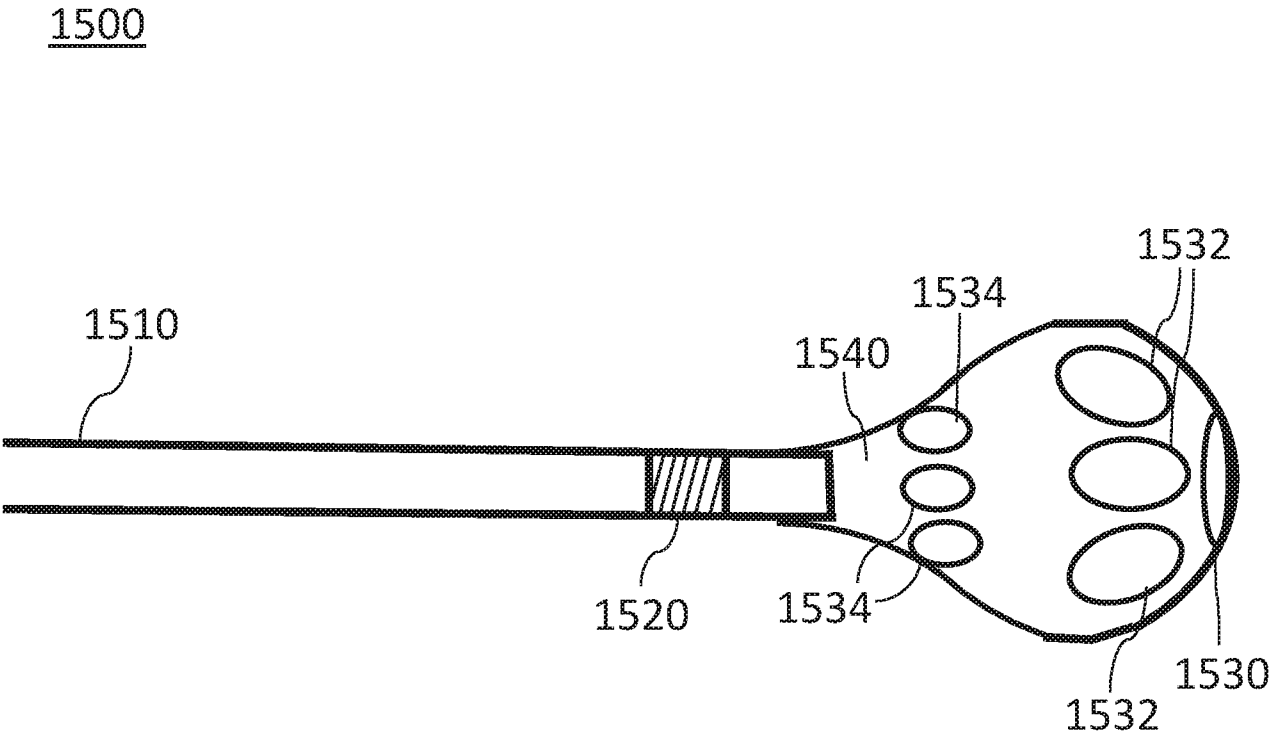


FIG. 15

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/050660

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/042 A61N1/32
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61N

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 245 064 B1 (LESH MICHAEL D [US] ET AL) 12 June 2001 (2001-06-12) column 6, line 61 - column 8, line 2; figures 8C-D, 9, 10A-11B column 17, lines 36-62 -----	1,3,4, 6-61
X	US 2017/105793 A1 (CAO HONG [US] ET AL) 20 April 2017 (2017-04-20) figures 1, 4 paragraphs [0036] - [0039] -----	2,6-61
X	US 2016/000500 A1 (SALAHIEH AMR [US] ET AL) 7 January 2016 (2016-01-07) paragraphs [0066] - [0069], [0075], [0139] - [0140]; figures 1A-B, 2A, 9A-B, 11A-12B, 31A-C, 37, 39 ----- -/-	3,5-61



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

16 November 2018

Date of mailing of the international search report

26/11/2018

Name and mailing address of the ISA/

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Authorized officer

Lahorte, Philippe

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/050660

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/030430 A1 (STEWART MARK T [US] ET AL) 31 January 2013 (2013-01-31) paragraphs [0036] - [0047]; figures 7-10, -----	1-61
A	WO 2017/120169 A1 (IOWA APPROACH INC [US]; PAGEARD JEAN-LUC [CA]) 13 July 2017 (2017-07-13) paragraphs [0049] - [0053], [0057] - [0058], [0062] - [0064], [0093] - [0097], [0116] - [0120]; figures 1-3, 6-7, 8A-B, 9A-11, 21-25 -----	1-61

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/050660

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 62-81
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 62-81

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery and therapy.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/050660

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6245064	B1	12-06-2001	NONE
US 2017105793	A1	20-04-2017	NONE
US 2016000500	A1	07-01-2016	AU 2014251039 A1 22-10-2015 CA 2908517 A1 16-10-2014 CN 105228547 A 06-01-2016 EP 2983603 A1 17-02-2016 HK 1219401 A1 07-04-2017 JP 2016515442 A 30-05-2016 KR 20150140760 A 16-12-2015 US 2014357956 A1 04-12-2014 US 2016000500 A1 07-01-2016 WO 2014168987 A1 16-10-2014
US 2013030430	A1	31-01-2013	CN 103781433 A 07-05-2014 EP 2736434 A1 04-06-2014 US 2013030430 A1 31-01-2013 US 2016051324 A1 25-02-2016 WO 2013019385 A1 07-02-2013
WO 2017120169	A1	13-07-2017	CN 108778173 A 09-11-2018 EP 3399933 A1 14-11-2018 WO 2017120169 A1 13-07-2017