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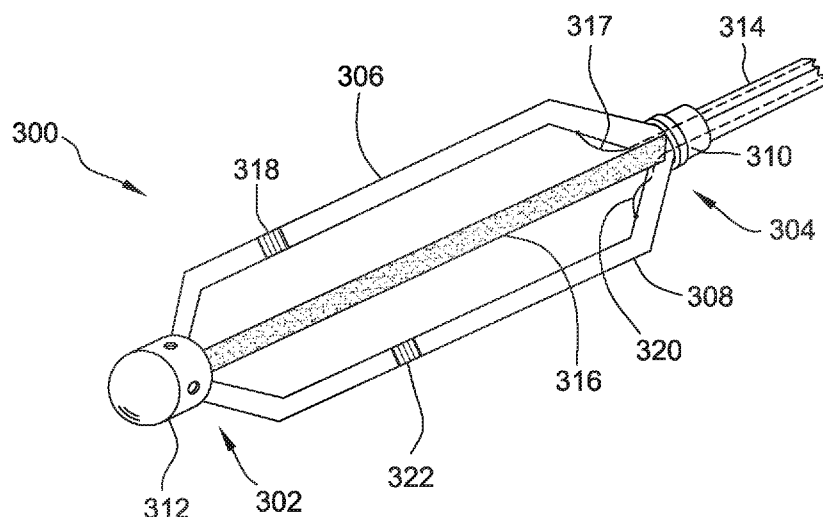


FIG. 2

(57) Abstract: The present disclosure provides catheter systems, electrode assemblies, and methods for electrically stimulating one or more points about the circumference of the renal artery to provide real time intraprocedural operational feedback to the operator of a renal denervation procedure to allow for more precise and thorough ablation of the renal artery and better patient outcomes. In many embodiments, an electrode assembly is provided that includes multiple splines that extend from an insulated proximal hub to an insulated distal hub and are interconnected to an electrical wire to allow the splines to independently function as electrical stimulation electrodes. The electrically active splines can then be energized at one or more desired points during a renal denervation procedure to provide operational feedback.



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CATHETER SYSTEM AND ELECTRODE ASSEMBLY FOR INTRAPROCEDURAL EVALUATION OF RENAL DENERVATION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/353,606, filed June 23, 2016, the contents of which are hereby incorporated by reference herein in their entirety.

A. Field of the disclosure

[0002] The present disclosure relates generally to catheter systems and methods for the intraprocedural evaluation of a renal denervation procedure. In particular, the present disclosure relates to a catheter system that includes an electrode assembly that has at least one electrically insulated spline that is interconnected with an electrical wire to allow the at least one spline to function as a stimulation electrode. The electrically active spline can provide electrical stimulation to the interior of the renal artery during a procedure to allow for operational feedback.

B. Background

[0003] Hypertension remains the most prevalent cardiovascular risk factor around the globe today. In humans, sympathetic nerve activity is increased in almost all forms of hypertension. Various renal denervation ablation procedures for the ablation of perivascular renal nerves in the renal arteries have been used for the treatment of hypertension, and specifically for drug-resistant hypertension. Generally, one or more radiofrequency electrodes are introduced into the body and fed into the renal artery and used to ablate the efferent and afferent nerves that generally run the length of the artery. In some cases, a single ablation procedure may include six to ten or more ablation areas along and around the wall of the artery. Typically, the operator performing the procedure will ablate one discrete area of the artery and then move the ablation electrode a desired distance lengthwise about the length of the artery and also rotate the handle of the catheter to move the ablation electrode circumferentially around the artery. In some cases, the operator may move the ablation electrode

circumferentially about 45 degrees around the artery wall between ablations. By varying the ablation treatment sites lengthwise down and circumferentially around the artery wall, any potential overall damage to the artery wall can be minimized or eliminated while the overall ablation of the efferent and afferent nerves can still be substantially complete and effective.

[0004] During the ablation procedure, the operator, typically a doctor, performing the procedure generally attempts to monitor and track all of the areas of the artery wall that have previously been ablated to avoid over-treatment of any one site. This monitoring and tracking is generally done both along the length of the artery as well as around the circumference of the artery wall to ensure proper ablation of the arterial nerves and the best procedural results. Feedback to the operator is generally provided regarding the temperature at the ablation site, which can also be indicative of the effectiveness of the ablation procedure itself, and whether the nerve has been ablated to a desired point.

BRIEF SUMMARY OF THE DISCLOSURE

[0005] The present disclosure provides catheter systems, electrode assemblies, and methods for electrically stimulating one or more points about the circumference of the renal artery to provide real time intraprocedural operational feedback to the operator of a renal denervation procedure to allow for more precise and thorough ablation of the renal artery and better patient outcomes. In many embodiments, an electrode assembly is provided that includes multiple splines that extend from an insulated proximal hub to an insulated distal hub and are interconnected to an electrical wire to allow the splines to independently function as electrical stimulation electrodes. The electrically active splines can then be energized at one or more desired points during a renal denervation procedure to provide electrical stimulation to the renal artery and operational feedback to the operator. Various embodiments of the present disclosure are set forth herein.

[0006] In one embodiment, the present disclosure is directed to a catheter system. The catheter system comprises: (i) a catheter shaft; and (ii) an electrode

assembly carried by the catheter shaft and including a proximal hub, a distal hub, and a first spline extending from the proximal hub to the distal hub, wherein the first spline includes a first ablation electrode thereon. The first spline is interconnected with an electrical wire to allow the first spline to function as a stimulation electrode.

[0007] In another embodiment, the present disclosure is directed to an electrode assembly. The electrode assembly comprises: (i) an electrically insulating proximal hub and an electrically insulating distal hub; (ii) a first spline extending from the electrically insulating proximal hub to the electrically insulating distal hub and carrying a first ablation electrode; and (iii) a second spline extending from the electrically insulating proximal hub to the electrically insulating distal hub and carrying a second ablation electrode. The first spline and the second spline are interconnected with an electrical wire to allow the first spline and the second spline to independently function as stimulation electrodes.

[0008] In another embodiment, the present disclosure is directed to a method of evaluating the intraprocedural success of a renal denervation procedure on a subject. The method comprises: (i) electrically stimulating multiple points about the circumference of a renal artery of the subject using at least one spline of an electrode assembly as a stimulation electrode to determine a baseline physiological response of the subject; (ii) performing a renal denervation procedure on the renal artery of the subject; (iii) electrically stimulating the multiple points about the circumference of the renal artery of the subject using at least one spline of an electrode assembly as a stimulation electrode to determine the physiological response of the subject; and (iv) comparing the baseline physiological response of the subject prior to renal denervation with the physiological response after renal denervation.

[0009] The foregoing and other aspects, features, details, utilities and advantages of the present disclosure will be apparent from reading the following description and claims, and from reviewing the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Figure 1 is a diagrammatic view of a renal denervation system for presenting information relating to lesion formation in a renal artery.

[0011] Figure 2 is a diagram of an electrode basket including two electrically active splines suitable for use in the present processes.

[0012] Figure 3 is a diagram of an electrode basket including four electrically active splines suitable for use in the present processes.

[0013] Figure 4 is a flow chart of one embodiment of a method for evaluating the intraprocedural success of a renal denervation procedure on a subject.

[0014] Figure 5 is a flow chart of one embodiment of a method of determining the end point of a renal denervation procedure on a subject.

[0015] Figure 6 is flow chart of one embodiment of a method of screening a subject for a renal denervation procedure.

[0016] Figure 7 is a flow chart of another embodiment of a method of screening a subject for a renal denervation procedure.

[0017] Figure 8 is a block diagram of a radiofrequency ablation generator modified to include electrical stimulation.

[0018] Corresponding reference characters indicate corresponding parts throughout the several views of the drawings. It is understood that that Figures are not necessarily to scale.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0019] The present disclosure provides catheter systems and electrode assemblies for use in methods for providing real time feedback to an operator, such as a doctor, performing a renal denervation procedure on a subject. These catheter systems and electrode assemblies provide at least one, and in many embodiments two,

three, four or more, electrically active splines that can be used to electrically stimulate the interior of the renal artery. The electrically active splines may also carry one or more ablation electrodes, thermocouples, or other electronic devices. By making one or more splines on the electrode basket electrically active, there is no need in many embodiments to provide additional electrical stimulation electrodes on the one of more splines to provide this functionality. The electrically active splines may be configured to operate independently of one another, and are generally secured to a proximal insulated hub and a distal insulated hub in the electrode assembly to allow the electrically active spline to be electrically insulated and electrically isolated.

[0020] In many embodiments, methods are provided for evaluating the intraprocedural confirmation of the end point of a renal denervation procedure such that the operator can assess the effectiveness of a procedure and decide whether additional renal denervation may be beneficial to the subject. Methods are also provided for screening subjects to determine whether the subject might benefit from a renal denervation procedure. The methods of the present disclosure utilize a modified ablation catheter including an electrode assembly having one or more electrically active splines in combination with ablation electrodes for electrical stimulation of multiple points about the circumference of the renal artery to provide intraprocedural feedback to the operator. In many embodiments, the multiple points about the circumference of the renal artery will include at least one point in each of the four quadrants of the renal artery. As used herein, “quadrant” refers to a circular section equal to one quarter of a circle such that the renal artery, which is generally circular in cross-section, would include four quadrants.

[0021] More specifically, many embodiments of the present disclosure utilize electrically active splines of an electrode basket to provide simultaneous or sequential electrical stimulation of multiple points about the circumference of the renal artery, or section thereof, prior to a renal denervation procedure to establish a baseline physiological response (such as a baseline blood pressure, baseline heart rate, baseline renal blood flow, or other physiological response as described herein) of a subject prior to any renal denervation taking place in the renal artery. By using

electrical stimulation of multiple points about the circumference of the renal artery, the physiological response is amplified due to the cumulative response of the multiple-point electrical stimulation as further described herein. The present methods significantly increase the likelihood of obtaining the true and accurate physiological response due to the electrical stimulation of multiple points about the circumference of the renal artery. Once the baseline physiological response has been established after electrical stimulation, the operator can perform a renal denervation procedure on the renal artery and then subsequently electrically stimulate the multiple points about the circumference of the renal artery again with the electrically active spline or splines of the electrode assembly to measure the physiological response of the subject after the renal denervation is complete. With this information, the operator can compare the physiological response before the renal denervation (after the first electrical stimulation) with the physiological response after renal denervation (after the second electrical stimulation), and determine, intraprocedurally, the effectiveness of the procedure and whether the subject may benefit from further denervation. The operator can also minimize both the number of ablations performed and the energy used, which can reduce or eliminate any potential damage to the renal artery and improve patient outcomes. Additionally, the real time information may allow for improved overall procedure management and efficiency. The methods of the present disclosure may further be utilized to screen potential renal denervation subjects to segregate those that might benefit from a renal denervation procedure from those that likely would not benefit.

[0022] The efferent and afferent nerves that lie within and immediately adjacent to the wall of the renal artery propagate longitudinally down the length of the renal wall in a non-uniform pattern that may be sometimes described as a spider-web or variable and non-predictable pattern. As such, it is generally difficult to determine the exact position of the efferent and afferent nerves of the renal artery. The methods of the present disclosure account for this irregular and unpredictable longitudinal propagation of the efferent and afferent nerves through the electrical stimulation of multiple points about the circumference of the renal artery using electrically active

electrode basket splines as described herein to elucidate the desired physiological response at the desired time of the procedure. By electrically stimulating at multiple points about the circumference of the renal artery using the electrically active splines, the ability to achieve sufficient electrical stimulation of the efferent and afferent nerves, and thus elicit a significant and measurable impact on the desired physiological response being evaluated, is significantly increased. The multiple point electrical stimulation results in a substantially increased likelihood of the electrical stimulation interacting with the desired nerves as a greater area of the renal artery is electrically stimulated. In many embodiments, it is desirable to have electrical stimulation occur in at least one location in each of the four quadrants of the renal artery; that is, it is desirable in some embodiments to electrically stimulate at least one location in each of the four quadrants of the renal artery. In many embodiments, the electrical stimulation points about the circumference of the renal artery may be equally spaced apart to reduce the potential of any damage to the renal artery and/or the efferent and afferent nerves.

[0023] For purposes of this description, the methods, systems, and apparatuses of the present disclosure will be primarily described in connection with the use of an ablation catheter and electrode assembly having two or four splines, with each spline being electrically active such that it may provide electrical stimulation to the interior of the renal artery. Some or all of the electrically active splines may include an ablation electrode. It is contemplated, however, that numerous other types of ablation catheters and electrode assemblies, including electrode assemblies having 3, 5, 6, 7, 8, 9, 10 or more splines, some or all of which being electrically active as described herein, can be used in the methods of the present disclosure as would be appreciated by one of ordinary skill in the art based on the disclosure herein.

[0024] Referring now to the Figures, Figure 1 illustrates one exemplary embodiment of a general ablation system 210 for performing one or more diagnostic and/or therapeutic functions that include components for presenting information representative of lesion formations in renal artery 214 during an ablation procedure performed thereon.

[0025] Among other components, system 210 includes a medical device (such as, for example, catheter 216), ablation system 218, and system 220 for the visualization, navigation, and/or mapping of internal body structures. System 220 may include, for example and without limitation, an electronic control unit (ECU) 222, display device 224, user input device 269, and memory 270. Alternatively, ECU 222 and/or display device 224 may be separate and distinct from, but electrically connected to and configured for communication with, system 220.

[0026] With continued reference to Figure 1, catheter 216 is provided for examination, diagnosis, and/or treatment of internal body tissues, such as renal artery 214. In an exemplary embodiment, catheter 216 comprises a radio frequency (RF) ablation catheter. It should be understood, however, that catheter 216 is not limited to an RF ablation catheter. Rather, in other embodiments, catheter 216 may comprise an irrigated catheter and/or other types of ablation catheters (e.g., cryoablation, ultrasound, etc.).

[0027] In an exemplary embodiment, catheter 216 is electrically connected to ablation system 218 to allow for the delivery of RF energy. Catheter 216 may include a cable connector or interface 230, handle 232, shaft 234 having a proximal end 236 and distal end 238 (as used herein, “proximal” refers to a direction toward the end of catheter 216 near the operator, and “distal” refers to a direction away from the operator and (generally) inside the body of a subject or patient), and one or more electrodes 240 mounted in or on shaft 234 of catheter 216. In an exemplary embodiment, electrode 240 is disposed at or near distal end 238 of shaft 234, with electrode 240 comprising an ablation electrode disposed at the extreme distal end 238 of shaft 234 for contact with renal artery 214. Catheter 216 may further include other conventional components such as, for example and without limitation, sensors, additional electrodes (e.g., ring electrodes) and corresponding conductors or leads, or additional ablation elements, e.g., a high intensity focused ultrasound ablation element and the like.

[0028] Connector 230 provides mechanical and electrical connection(s) for cables 248 and 250 extending from ablation system 218, and visualization, navigation, and/or mapping system 220. Connector 230 is conventional in the art and is disposed at the proximal end of catheter 216.

[0029] Handle 232 provides a location for the operator to hold catheter 216 and may further provide means for steering or guiding shaft 234 within renal artery 214. For example, handle 232 may include means to change the length of a guidewire extending through catheter 216 to distal end 238 of shaft 234 to steer shaft 234. Handle 232 is also conventional in the art and it will be understood that the construction of handle 232 may vary. In another exemplary embodiment, catheter 216 may be robotically driven or controlled. Accordingly, rather than an operator manipulating a handle to steer or guide catheter 216, and shaft 234 thereof, in particular, a robot is used to manipulate catheter 216.

[0030] Shaft 234 is generally an elongated, tubular, flexible member configured for movement within renal artery 214. Shaft 234 supports, for example and without limitation, electrode 240, associated conductors, and possibly additional electronics used for signal processing or conditioning. Shaft 234 may also permit transport, delivery and/or removal of fluids (including irrigation fluids, cryogenic ablation fluids, and bodily fluids), medicines, and/or surgical tools or instruments. Shaft 234 may be made from conventional materials such as polyurethane, and defines one or more lumens configured to house and/or transport at least electrical conductors, fluids, or surgical tools. Shaft 234 may be introduced into renal artery 214 through a conventional introducer. Shaft 234 may then be steered or guided through renal artery 214 to a desired location with guidewires or other means known in the art.

[0031] With further reference to Figure 1, ablation system 218 is comprised of, for example, ablation generator 252. Ablation generator 252 generates, delivers, and controls RF energy output by ablation catheter 216 and electrode 240 thereof, in particular. In an exemplary embodiment, generator 252 includes RF ablation signal

source 256 configured to generate an ablation signal that is output across a pair of source connectors: a positive polarity connector SOURCE (+), which may be electrically connected to tip electrode 240 of catheter 216; and a negative polarity connector SOURCE (-). It should be understood that the term connectors as used herein does not imply a particular type of physical interface mechanism, but is rather broadly contemplated to represent one or more electrical nodes. Source 256 is configured to generate a signal at a predetermined frequency in accordance with one or more user specified parameters (e.g., power, time, etc.) and under the control of various feedback sensing and control circuitry as is known in the art. Source 256 may generate a signal, for example, with a frequency of about 450 kHz or greater. Generator 252 may also monitor various parameters associated with the ablation procedure including, for example, impedance, the temperature at the distal tip of the catheter, applied ablation energy, and the position of the catheter, and provide feedback to the clinician or another component within system 210 regarding these parameters.

[0032] In accordance with the present disclosure, ablation catheters suitable for use in the processes and systems described herein for the evaluation of the intraprocedural success of a renal denervation procedure and/or patient screening include an electrode assembly wherein one or more of the splines are electrically active; that is, wherein one or more of the splines of the electrode assembly are electrically insulated and isolated and are capable of providing electrical stimulation to the interior of the renal artery independent of any other component. The electrically active splines will also in many embodiments each also include at least one ablation electrode thereon, and may optionally include a thermocouple and/or other sensors or electronic devices. The exact type and design of the ablation catheter and electrode basket is not critical so long as the ablation catheter and electrode basket is configured to allow for at least one spline to be electrically active so as to provide electrical stimulation at about the circumference of the renal artery. In some embodiments, the ablation catheter is sized and configured with electrically active splines to allow for electrical stimulation of at least 2, or even 3, or even 4 or even 5

or even 6 or even 7 or even 8 or more points about the circumference of the renal artery. In many embodiments, the ablation catheter is sized and configured such that the electrical stimulation at multiple points is generally equally spaced apart about the circumference of the renal artery. In one specific embodiment, the ablation catheter is sized and configured to allow for electrical stimulation at one point within each of the four quadrants of the renal artery. Such four quadrant electrical stimulation may desirably be equally spaced apart in many embodiments. Many types of ablation catheters may be configured in this manner and are suitable for use in accordance with the present disclosure including, for example, multiple spline catheters (i.e., electrode baskets having 2, 3, 4, 5, 6, or more splines), spiral catheters, balloon catheters, and the like).

[0033] Referring now to Figure 2, there is illustrated an electrode basket in accordance with one embodiment of the present disclosure that is suitable for use with an ablation catheter in the methods of the present disclosure. Electrode basket 300 has a distal end 302 and a proximal end 304 and includes electrically active spline 306 and electrically active spline 308. Electrically active splines 306 and 308 are connected to a proximal insulated hub 310 and a distal insulated hub 312 in order to electrically insulate and isolate electrically active splines 306 and 308. Proximal insulated hub 310 and distal insulated hub 312 may be constructed from any suitable electrically insulating material including, for example, polymeric materials and thermoplastic materials including Ultem™ or another polyetherimide. Other high temperature liquid crystal polymers are also suitable for use in the construction of proximal insulated hub 310 and distal insulated hub 312. Electrode basket 300 also includes elongated catheter body 314 through which pulling wire 316 runs through and connects to distal insulated hub 312. Pulling wire 316 can be used to expand/contract electrode basket 300 into different conformations before, during, and after an ablation procedure. Also running through elongated catheter body 314 is electrical wire 317 which is electrically connected to electrically active spline 306 and electrical wire 320 which is electrically connected to electrically active spline 308. Electrical wire 317 and electrical wire 320 are connected to an electrical source (not

shown) such that they can carry electricity to electrically active spline 306 and electrically active spline 308 such that electrically active spline 306 and electrically active spline 308 are electrically active and capable of providing electrical stimulation as described herein.

[0034] With continued reference to Figure 2, electrically active spline 306 and electrically active spline 308 of electrode basket 300 each include ablation electrode 318 and 322, respectively. Ablation electrodes 318 and 322 are positioned on electrically active spline 306 and electrically active spline 308, respectfully to allow contact thereof with different quadrants of a renal artery (not shown in Figure 2 but see Figure 1) after insertion and expansion therein. Each of ablation electrodes 318 and 322 are electrically insulated (electrical insulation not shown in Figure 2) from electrically active spline 306 and electrically active spline 308 to ensure that each electrical component can act independently and without short circuits or other electrical interference problems. In many embodiments, the same material of construction may be used for electrically active splines 306 and 308 and for ablation electrodes 318 and 322. Suitable materials may include, for example, gold and alloys thereof, platinum and alloys thereof, stainless steel and alloys thereof, and metal alloys of nickel and titanium and combinations thereof.

[0035] Referring now to Figure 3, there is illustrated an electrode basket in accordance with one embodiment of the present disclosure that is suitable for use with an ablation catheter in methods of the present disclosure. Electrode basket 400 includes four electrically active splines 402, 404, 406, and 408 each connected to distal insulated hub 410 and proximal insulated hub 412. Electrode basket 400 also includes elongated catheter body 414 through which pulling wire 413 runs through and connects to distal insulated hub 410. Pulling wire 413 can be used to expand/contract electrode basket 400 into different conformations before, during, and after an ablation procedure. Also running through elongated catheter body 414 is electrical wire 416 which is electrically connected to electrically active spline 402, electrical wire 418 which is electrically connected to electrically active spline 404, electrical wire 420 which is electrically connected to electrically active spline 406 and

electrical wire 422 which is electrically connected to electrically active spline 408. Electrical wire 416, electrical wire 418, electrical wire 420, and electrical wire 422 are each connected to an electrical source (not shown) such that they can carry electricity to electrically active spline 402, electrically active spline 404, electrically active spline 406, and electrically active spline 408 such that electrically active spline 402, electrically active spline 404, electrically active spline 406 and electrically active spline 408 are electrically active and capable of providing electrical stimulation as described herein. Although illustrated in Figure 3 as four separate electrical wires, it will be recognized by one skilled in the art based on the disclosure herein that other electrical configurations, such as a single wire attached to all four electrically active splines, are within the scope of the present disclosure.

[0036] With continued reference to Figure 3, electrically active spline 402, electrically active spline 404, electrically active spline 406, and electrically active spline 408 of electrode basket 400 each include ablation electrode 424, 426, 428, and 430, respectively. Ablation electrodes 424, 426, 428, and 430 are positioned on electrically active spline 402, electrically active spline 404, electrically active spline 406, and electrically active spline 408 to allow contact thereof with each quadrant of a renal artery (not shown in Figure 3 but see Figure 1) after insertion and expansion therein. Each of ablation electrodes 424, 426, 428, and 430 are electrically insulated (electrical insulation not shown in Figure 3) from electrically active spline 402, electrically active spline 404, electrically active spline 406, and electrically active spline 408 to ensure that each electrical component can act independently and without short circuits or other electrical interference problems.

[0037] In accordance with many embodiments of the present disclosure, a single electrically active spline on an electrode basket may be used with the ablation electrode mounted thereon as a bipolar pair for electrical stimulation of the interior of the renal artery. In other embodiments, two adjacent, or two opposed, electrically active splines may be used as a bipolar pair for spline to spline electrical stimulation of the interior of the renal artery. In other embodiments, one or more electrically active splines can be coupled to a body patch and used as a bipolar pair for electrical

stimulation of the interior of the renal artery. In many embodiments, the one or more pairs of electrically active splines are sequentially stimulated, although simultaneous stimulation is within the scope of the present disclosure as discussed herein.

[0038] In one exemplary embodiment of the present disclosure, the bipolar electrical stimulation to the interior of the renal artery is provided through sequential electrical stimulation of electrically active splines 402 and 406 followed by electrically active splines 404 and 408, followed by electrically active splines 402 and 406, and followed by electrically active spline 404 and 408, etc. Other bipolar sequential stimulation patterns are also within the scope of the present disclosure.

[0039] In some embodiments of the present disclosure, the electrically active splines as described herein are configured such that the entire spline may act as an electrical stimulation electrode; that is, the spline is configured such that the entire length of the spline is electrically active. In other embodiments of the present disclosure, the spline may be configured such that only a portion, or portions, of the spline is capable of functioning as an electrical stimulation electrode. In these embodiments, the spline may include one or more areas that are electrically isolated or insulated such that these areas do not conduct electricity and cannot function as an electrical stimulation site. In some embodiments, only one quarter, or one half, or even only three quarters of the length of the spline will be electrically active, with the remaining lengthwise portions being electrically insulated or isolated.

[0040] As discussed in further detail herein, the electrical stimulation provided by the one or more electrically active splines as described herein is desirably at an intensity level sufficient to elicit the desired physiological response in the subject, but is not too intense as to potentially damage the renal artery or nerves therein or introduce a high level of pain to the subject; that is, the electrical stimulation provided by the one or more electrically active splines to the multiple points about the circumference of the renal artery should not be too diffuse or too intense.

[0041] In accordance with various embodiments of the present disclosure, ablation catheters including electrode assemblies having one or more splines capable of providing electrical stimulation may be used in methods described herein for the evaluation of the intraprocedural success of a renal denervation procedure on a subject; that is, electrical stimulation to the renal artery at prescribed times as described herein may be used to provide real time feedback to the operator of a renal denervation procedure on a subject to allow the operator to determine how successful a renal denervation procedure on the subject has been, and determine whether further denervation may be beneficial or desirable. Other embodiments allow for methods of screening patients for renal denervation procedures. A number of exemplary methods of the present disclosure are set forth in Figures 4-7 and described in more detail hereinbelow.

[0042] Figure 4 is a flow chart of one embodiment of a method 700 for evaluating the intraprocedural success of a renal denervation procedure. Method 700 includes electrically stimulating 702 multiple points about the circumference of a renal artery of a subject to determine a baseline physiological response of the subject; performing 704 a renal denervation procedure on the renal artery of the subject; electrically stimulating 706 the multiple points about the circumference of the renal artery of the subject to determine the physiological response of the subject; and comparing 708 the baseline physiological response of the subject prior to the renal denervation with the physiological response after the renal denervation.

[0043] Figure 5 is a flow chart of one embodiment of a method 800 for determining the end point of a renal denervation procedure on a subject. Method 800 includes electrically stimulating 802 multiple points about the circumference of a renal artery of the subject through electrical stimulation to determine a baseline reading of the subject's blood pressure using an ablation catheter comprising at least four ablation electrodes located on four electrically active splines configured to electrically contact the renal artery; performing 804 a renal denervation procedure on the renal artery of the subject using the ablation catheter; electrically stimulating 806 the multiple points about the circumference of the renal artery of the subject through

electrical stimulation using an ablation catheter configured to electrically contact the renal artery to determine the subject's blood pressure; comparing 808 the baseline blood pressure of the subject prior to renal denervation with the blood pressure after renal denervation; and determining 810 whether to perform an additional renal denervation procedure.

[0044] Figure 6 is a flow chart of one embodiment of a method 900 of screening a subject for a renal denervation procedure. Method 900 includes electrically stimulating 902 the four quadrants of a renal artery of the subject through electrical stimulation using an ablation catheter configured to electrically contact the four quadrants of the renal artery to determine a baseline reading of the subject's blood pressure and determining 904 whether the baseline reading meets a threshold indicating that the subject may benefit from a renal denervation procedure.

[0045] Figure 7 is a flow chart of one embodiment of a method 950 of screening a subject for a renal denervation procedure. Method 950 includes electrically stimulating 952 the four quadrants of a renal artery of the subject through sequential or simultaneous electrical stimulation using an ablation catheter configured to electrically contact the four quadrants of the renal artery to determine a baseline reading of the subject's blood pressure; performing 954 a renal denervation procedure on the renal artery of the subject using the ablation catheter; electrically stimulating 956 the four quadrants of the renal artery of the subject through sequential or simultaneous electrical stimulation using an ablation catheter configured to electrically contact the four quadrants of the renal artery to determine the subject's blood pressure; comparing 958 the baseline blood pressure of the subject prior to renal denervation with the blood pressure after renal denervation; and determining 960 whether the subject may benefit from additional renal denervation.

[0046] In order to evaluate the intraprocedural success of a renal denervation procedure and/or perform patient screening, a baseline physiological response of the subject is first measured and recorded prior to any renal denervation occurring on the subject. A "baseline physiological response" refers to the response elicited by a

subject after electrical stimulation of the multiple points about the circumference of the renal artery; for example, a baseline blood pressure would be the blood pressure determined after electrical stimulation. A number of physiological responses may be selected for measuring prior to the renal denervation procedure to establish a baseline reading that is later compared against another reading after renal denervation as described herein. Further examples include blood pressure, heart rate, renal blood flow, catecholamine (epinephrine and norepinephrine) level, heart rate variability, natriuresis, and other biomarker levels, and combinations thereof. In many embodiments, blood pressure is a desired physiological response to measure as a baseline as it can easily be measured outside of the subject's body throughout the course of the procedure. As used herein, the term "blood pressure" encompasses systolic blood pressure, diastolic blood pressure and mean blood pressure. Any of systolic blood pressure, diastolic blood pressure and mean blood pressure may be suitably used as a physiological response in accordance with the present disclosure. In some embodiments, two or more physiological responses may be measured.

[0047] The baseline physiological response of the subject is measured by first electrically stimulating multiple points about the circumference of the renal artery (or parts thereof as discussed below) using one or more electrically active splines on the electrode assembly as described above. As noted, the electrical stimulation at the multiple points about the circumference of the renal artery may be equally spaced about the circumference of the renal artery to lessen any chance of damage to the artery and/or the nerves due to over-stimulation. The renal artery may be stimulated about its circumference at 2, 3, 4, 5, 6, 7, 8 or more points to increase the likelihood that the efferent and afferent nerves are sufficiently electrically stimulated so as to provide the desired physiological response. In one particular embodiment, the electrical stimulation using the electrically active electrode basket splines occurs at a single point within each of the four quadrants of the renal artery, such that there are four electrical stimulation points (corresponding to the four quadrants of the renal artery) about the circumference of the renal artery, that may be desirably equally spaced apart about the circumference.

[0048] The stimulation parameters for the electrical stimulation for the electrically active splines to set include the current, pulse width, and frequency. At a particular fixed setting, the stimulation as described herein is generally performed for a time period of from about 60 seconds to about 120 seconds. The current and pulse rate can be varied to bring about the desired physiological response from the patient. The methods of the present disclosure provide improved reliability and consistency due to the fact that multiple points about the circumference of the renal artery are electrically stimulated (either sequentially or simultaneously with the electrically active spline(s)) to elicit the desired physiological response. As discussed herein, by electrically stimulating multiple points about the circumference of the renal artery, there is a significantly increased confidence level that the desired afferent and/or efferent renal artery nerves are stimulated to elicit the desired physiological response.

[0049] There are numerous sites within the renal artery that are suitable for the electrical stimulation to occur. Suitable sites within the renal artery include, for example, unilateral sites, bilateral sites, the length of the renal artery, near the ostium, near the bifurcation, renal arterial branches distal to the bifurcation, intra-renal artery branches, and combinations thereof. Prior to stimulation, in some cases the doctor or operator may monitor the blood pressure of the patient over a period of time from about 60 seconds to 120 seconds so as to understand the blood pressure patterns and typical variation in blood pressure prior to electrical stimulation. In many cases, the more the baseline blood pressure rises as a result of the electrical stimulation, the more effective a renal denervation procedure may be for the patient as this is indicative of active nerve pathways in the renal artery.

[0050] In some embodiments, the electrical stimulation within the renal artery may be performed using sequential (multiplexing) electrical stimulation; that is, the electrical stimulation provided to the nerves may be sequential in nature wherein one electrically active spline is energized, followed by the second, then the third, then the fourth, etc. Also, as noted, the electrically active splines may be energized in pairs such that a first pair is energized followed by a second pair, etc. When sequential electrical stimulation is employed, the physiological response measured is

the cumulative physiological response generated by the electrical stimulation in total as the sequential firing is done very quickly as described herein. In other embodiments, the electrical stimulation within the renal artery may be performed using simultaneous electrical stimulation wherein all electrically active splines are energized at the same time such that the electrical stimulation to all four quadrants of the artery is provided at the same time. In some embodiments as described herein, sequential (multiplexing) electrical stimulation may be desirable as this type of electrical stimulation may result in a reduced chance of over-stimulation of the nerves.

[0051] The electrical stimulation provided to the renal artery by the electrically active splines generally provides a current in an amount of from about 0.1 milliamps to about 40 milliamps, including from about 10 milliamps to about 25 milliamps. This electrical current is supplied at a frequency of from about 1 Hertz to about 50 Hertz, including from about 15 Hertz to about 20 Hertz. The electrical current is generally supplied for a time period of from about 1 millisecond to about 25 milliseconds, including from about 1 millisecond to about 5 milliseconds, including from about 1 millisecond to about 2 milliseconds. The time between electrical stimulations may be from about 1 millisecond to about 10 milliseconds. In some embodiments, the electrical stimulation provided to the subject may be monopolar in nature (monopolar mode) between the electrically active spline and an indifferent electrode patch placed on the subject during a renal denervation procedure. In other embodiments as noted above, the electrical stimulation provided to the subject may be bipolar in nature (bipolar mode) between the electrically active spline and the adjacent electrically active spline or between two electrically active splines. Because renal nerves generally traverse primarily longitudinally along the length of the renal artery, in many embodiments bipolar electrical stimulation may be desirable and effective in depolarizing the nerves.

[0052] The electrical stimulation described herein may be delivered to the subject as rectangular pulse waves, triangular pulse waves, sinusoidal pulse waves, Gaussian pulse waves, and combinations thereof. The electrical stimulation wave

forms may include monophasic, charge balanced, and imbalanced biphasic, all of which may be delivered with or without delay. In some embodiments, it is desirable to provide the electrical stimulation in the form of rectangular pulse waves in a multiplexing manner from the pairs of electrically active splines.

[0053] In some embodiments of the present disclosure, it may be desirable to integrate the electrical stimulation functionality of the splines into the radiofrequency or ultrasound generator, or any other generator with an energy source, that is utilized to provide the ablation aspects of the renal denervation procedure so that only a single generator unit is required for the procedure. Referring now to Figure 8, there is shown one exemplary radiofrequency ablation generator block diagram with an electrical stimulation module (for connection with the one or more electrically active splines) integrated therein. Figure 8 illustrates the circuits in one embodiment that would allow the electrical stimulation functionality into a radiofrequency system. Specifically system 500 may include AC/DC power module 502 for accepting AC power in that provides DC power to a central processing unit (CPU) 504 that is in electrical communication with a USB port 506, Footswitch 508 and a display and user interface module 511. AC/DC power module 502 is also in communication with fan 510. Central processing unit 504 is further in electrical communication with a radiofrequency power amplifier/stimulation module 512 for supplying radiofrequency energy and electrical energy to the electrodes of an ablation catheter (not shown in Figure 8), and thermo module 514. A patient connection 516 is in electrical contact with thermo module 514 and radiofrequency power amplifier/stimulation module 512. An indifferent electrode patch on the subject 518 is also in electrical communication with radiofrequency power amplifier/stimulation module. Of course, the electrical stimulation function as described herein may be provided to the subject in any number of other ways and methods in accordance with the present disclosure.

[0054] Once the baseline physiological response of the subject has been measured through the electrical stimulation of the multiple points about the circumference of the renal artery as described above and a sufficient time has passed to allow for the physiological response to return to normal (generally at least 1

minute, or 2 minutes, or 3 minutes, or 4 minutes or even 5 minutes), the operator may then perform the renal denervation procedure on the renal artery of the subject. In some cases, the operator may determine that the electrical stimulation of the renal artery did not elicit a suitable physiological response from the subject and may determine that the particular subject is not a good candidate for a renal denervation procedure; that is, the methods of the present disclosure may also allow an operator to screen subjects prior to the renal denervation procedure to determine whether the particular subject may benefit from the renal denervation procedure.

[0055] After the operator has completed the renal denervation procedure in the renal artery, the renal artery is then again electrically stimulated at multiple points about its circumference as described herein and the physiological response of the subject determined. Generally, it is desirable to provide the electrical stimulation after renal denervation in the same area where the electrical stimulation was provided to determine the baseline physiological response. It should be noted, however, that the stimulation after renal denervation could be made at a different location. The operator can then compare the baseline physiological response (that is, the physiological response generated by the subject prior to any renal denervation due to the electrical stimulation) to the physiological response generated after the renal denervation procedure and determine the effectiveness of the renal denervation procedure. This intraprocedural feedback then allows the operator to determine, in real time and based on the physiological responses of the subject, whether any additional renal denervation may benefit the subject or whether the procedure should be ended. In the event that the operator determines that additional renal denervation may benefit the subject, a further renal denervation procedure may be done and another subsequent physiological response based on electrical stimulation performed and again evaluated against the baseline physiological response. In some embodiments, it may be beneficial for a second renal denervation procedure to be performed if the blood pressure of the subject in response to the electrical stimulation has not been reduced by at least about 20%, or even at least about 30%, or even at least about 40%, or even at least about 50%, without causing hypotension. In many

embodiments, a second renal denervation procedure may be desirable if the blood pressure on the subject in response to the electrical stimulation has not been reduced by at least about 10% after the first renal denervation procedure.

[0056] Although certain embodiments of this disclosure have been described above with a certain degree of particularity, those skilled in the art could make numerous alterations to the disclosed embodiments without departing from the spirit or scope of this disclosure. All directional references (e.g., upper, lower, upward, downward, left, right, leftward, rightward, top, bottom, above, below, vertical, horizontal, clockwise, and counterclockwise) are only used for identification purposes to aid the reader's understanding of the present disclosure, and do not create limitations, particularly as to the position, orientation, or use of the disclosure. Joinder references (e.g., attached, coupled, connected, and the like) are to be construed broadly and may include intermediate members between a connection of elements and relative movement between elements. As such, joinder references do not necessarily infer that two elements are directly connected and in fixed relation to each other. It is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative only and not limiting. Changes in detail or structure may be made without departing from the spirit of the disclosure as defined in the appended claims.

[0057] When introducing elements of the present disclosure or the preferred embodiment(s) thereof, the articles "a", "an", "the", and "said" are intended to mean that there are one or more of the elements. The terms "comprising", "including", and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

[0058] As various changes could be made in the above constructions without departing from the scope of the disclosure, it is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense.

WHAT IS CLAIMED IS:

1. A catheter system comprising:

a catheter shaft; and

an electrode assembly carried by the catheter shaft and including a proximal hub, a distal hub, and a first spline extending from the proximal hub to the distal hub, wherein the first spline includes a first ablation electrode thereon; and

wherein the first spline is interconnected with an electrical wire to allow the first spline to function as a stimulation electrode.
2. The catheter system of claim 1, wherein the first hub and the second hub are constructed from an electrically insulating material.
3. The catheter system of claim 2, wherein the insulating material is a high temperature liquid crystal polymer.
4. The catheter system of claim 1, wherein the first spline and the first ablation electrode are constructed from the same material.
5. The catheter system of claim 4, wherein the first spline and the first ablation electrode are constructed from a metal alloy of nickel and titanium.
6. The catheter system of claim 1, further comprising a second spline that includes a second ablation electrode.
7. An electrode assembly comprising:

an electrically insulating proximal hub and an electrically insulating distal hub;

a first spline extending from the electrically insulating proximal hub to the electrically insulating distal hub and carrying a first ablation electrode; and

a second spline extending from the electrically insulating proximal hub to the electrically insulating distal hub and carrying a second ablation electrode;

wherein the first spline and the second spline are interconnected with an electrical wire to allow the first spline and the second spline to independently function as stimulation electrodes.

8. The electrode assembly of claim 7, further comprising:

a third spline extending from the proximal hub to the distal hub and carrying a third ablation electrode; and

a fourth spline extending from the proximal hub to the distal hub and carrying a fourth ablation electrode.

9. The electrode assembly of claim 8, wherein the third spline and the fourth spline are interconnected with an electrical wire to allow the third spline and the fourth spline to independently function as stimulation electrodes.

10. A method of evaluating the intraprocedural success of a renal denervation procedure on a subject, the method comprising:

electrically stimulating multiple points about the circumference of a renal artery of the subject using at least one spline of an electrode assembly as a stimulation electrode to determine a baseline physiological response of the subject;

performing a renal denervation procedure on the renal artery of the subject;

electrically stimulating the multiple points about the circumference of the renal artery of the subject using at least one spline of an electrode assembly as a stimulation electrode to determine the physiological response of the subject; and

comparing the baseline physiological response of the subject prior to renal denervation with the physiological response after renal denervation.

11. The method of claim 10 wherein the electrical stimulation of the renal artery and the renal denervation are performed using the same electrode assembly.
12. The method of claim 10 wherein the electrode assembly comprises at least four electrically active splines and at least four ablation electrodes
13. The method of claim 10 wherein the electrical stimulation is performed using sequential electrical stimulation.
14. The method of claim 10 wherein the electrical stimulation is performed using simultaneous electrical stimulation.
15. The method of claim 10 wherein the electrical stimulation is bipolar electrical stimulation.

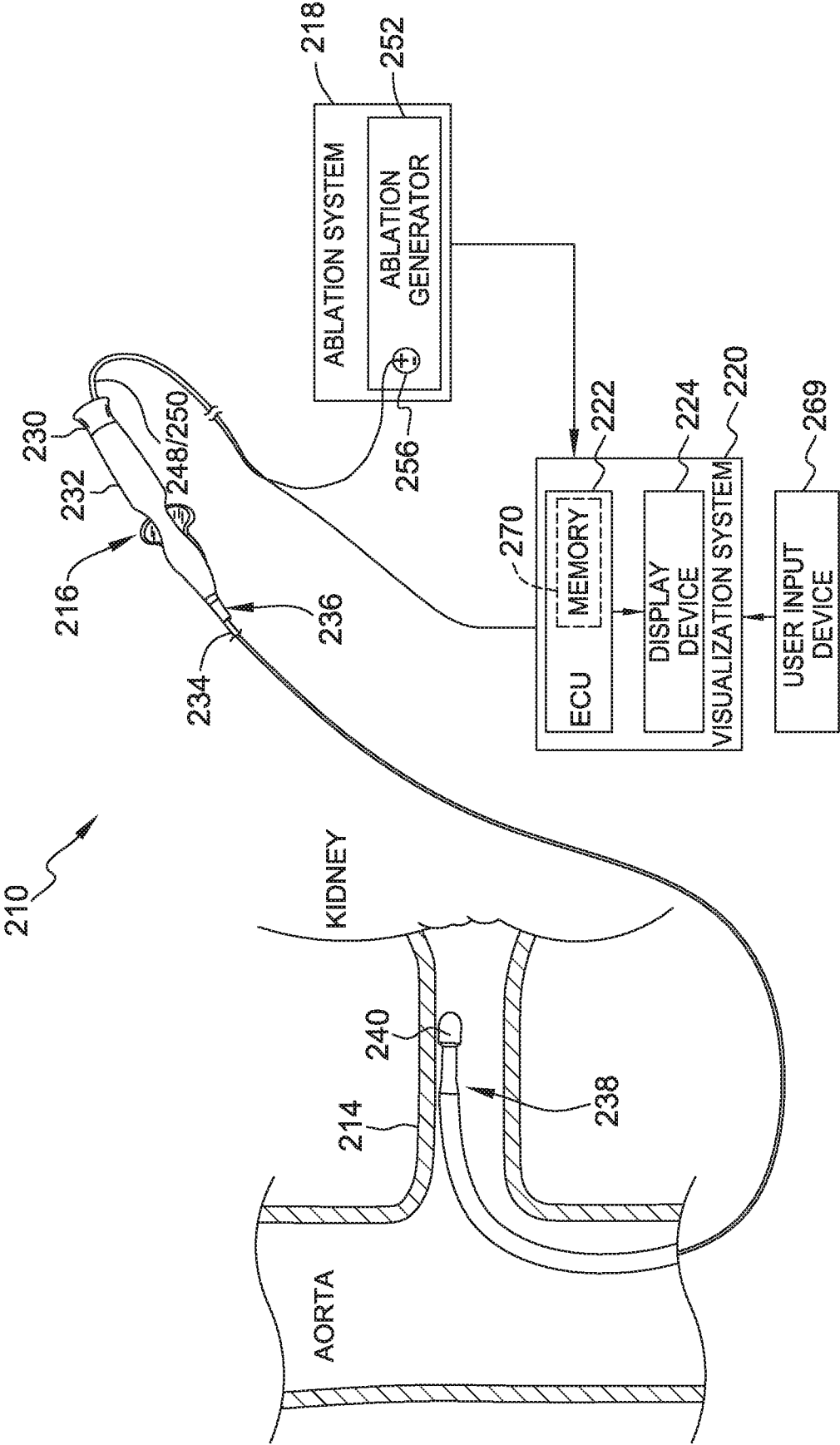


FIG. 1

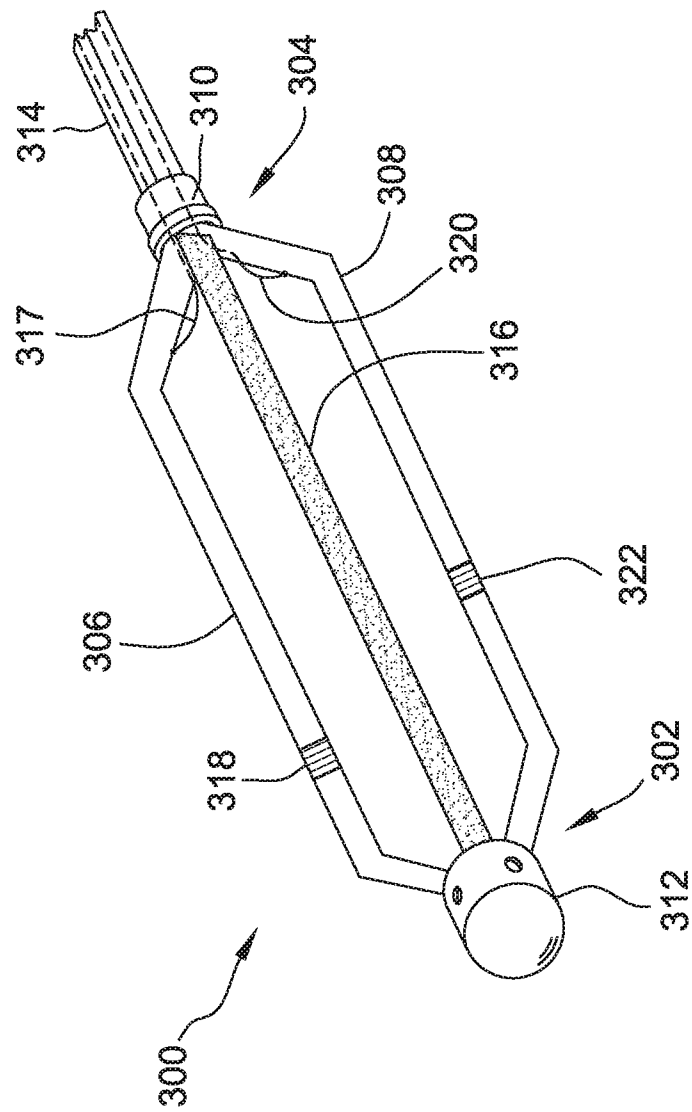


FIG. 2

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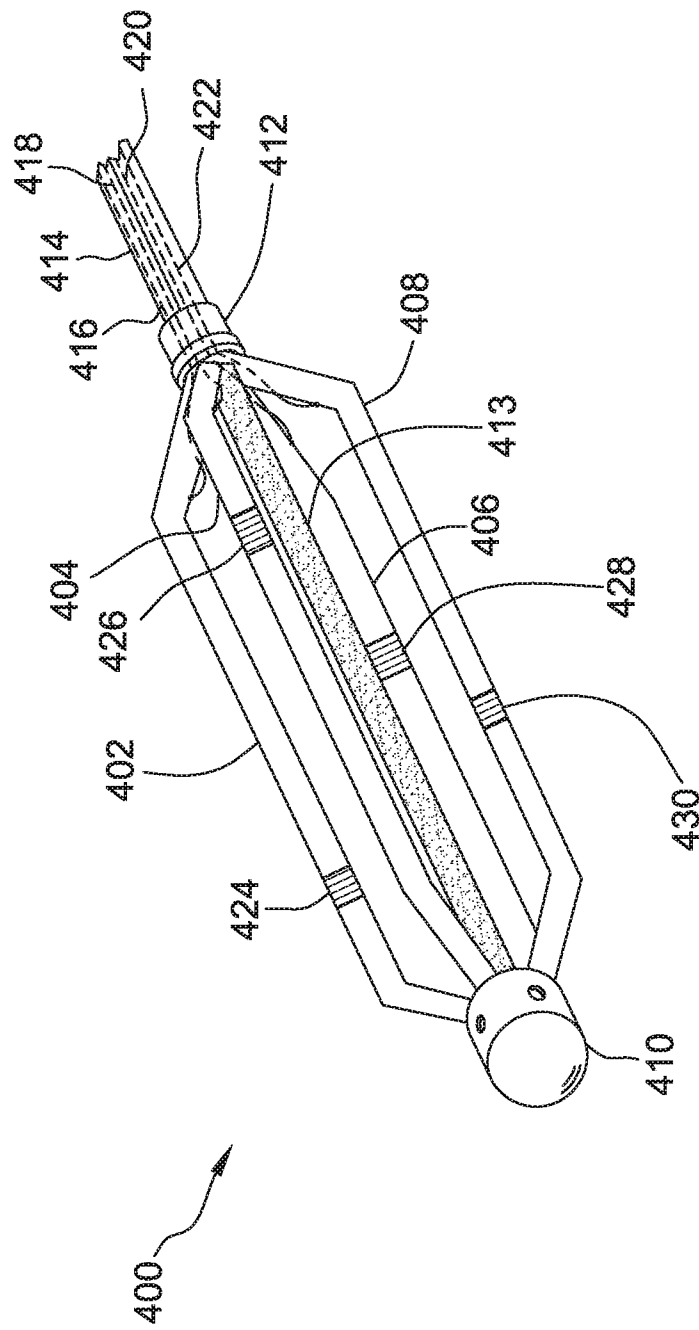


FIG. 3

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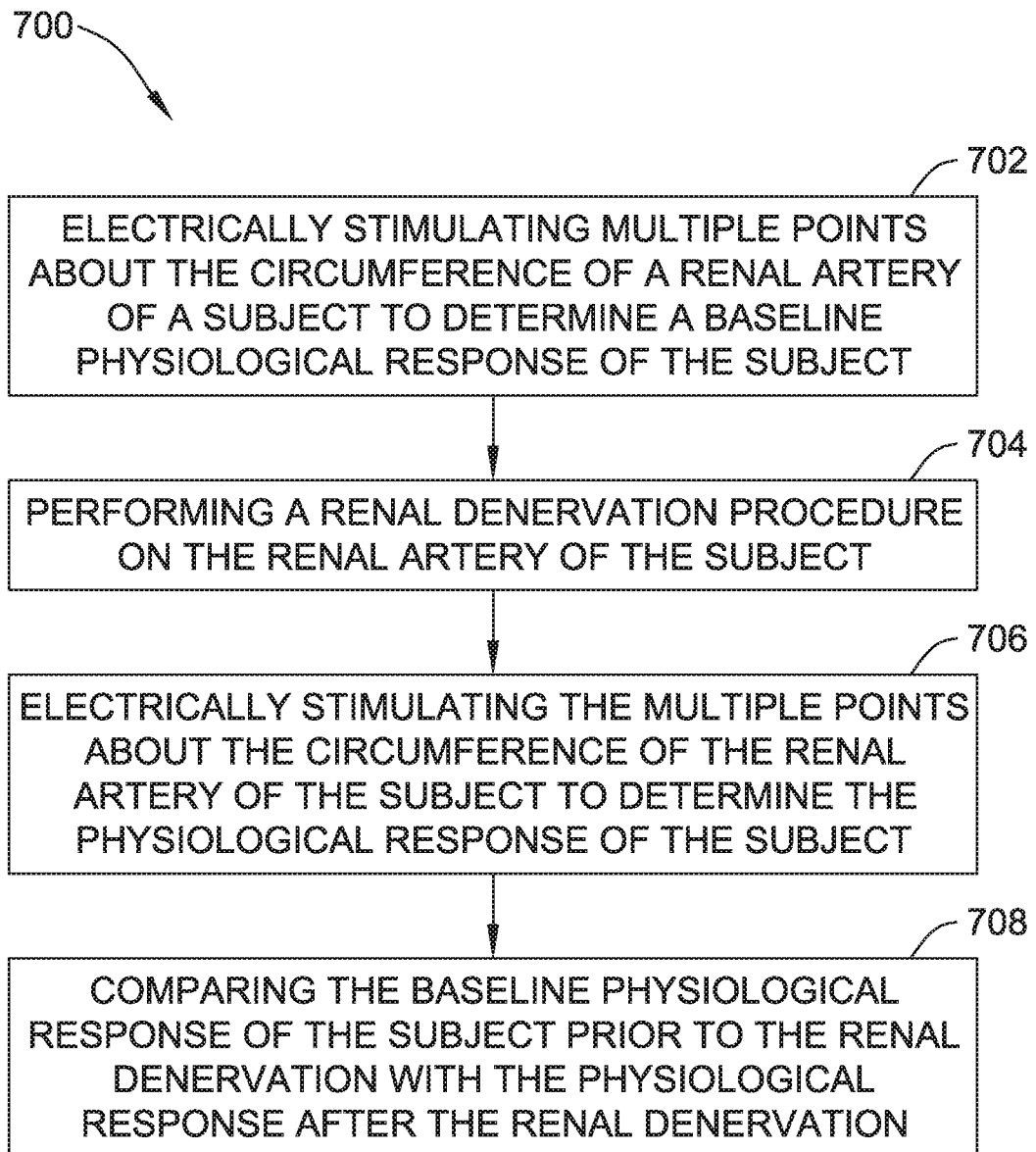


FIG. 4

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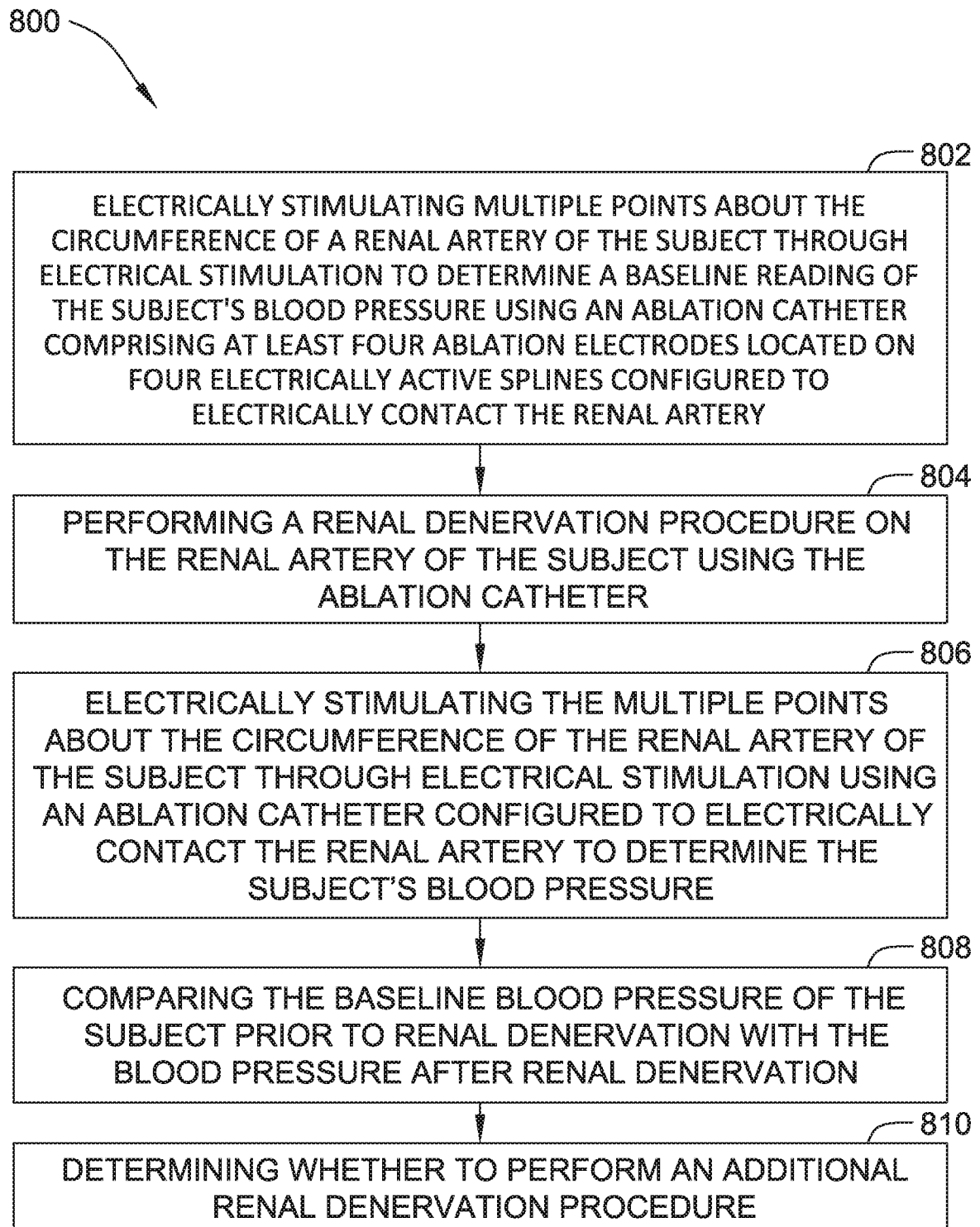


FIG. 5

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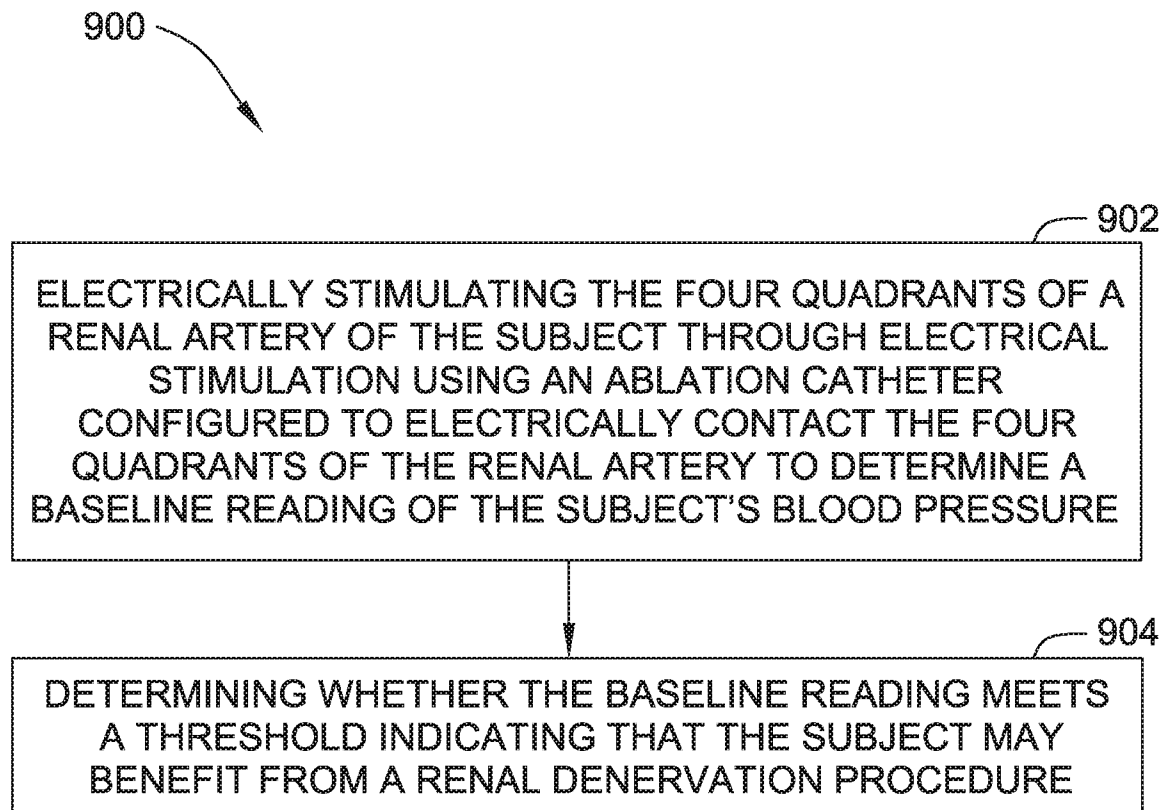


FIG. 6

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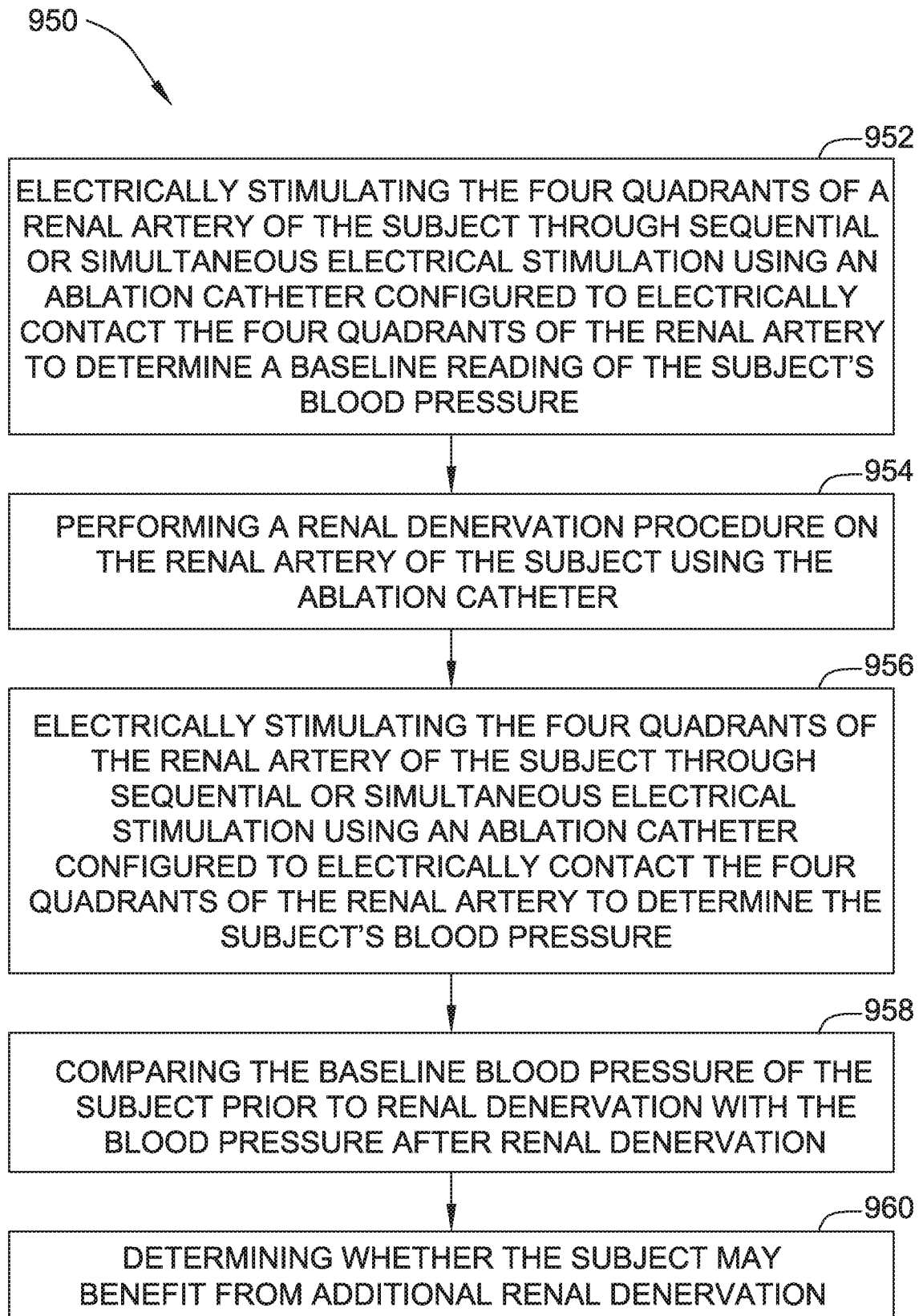


FIG. 7

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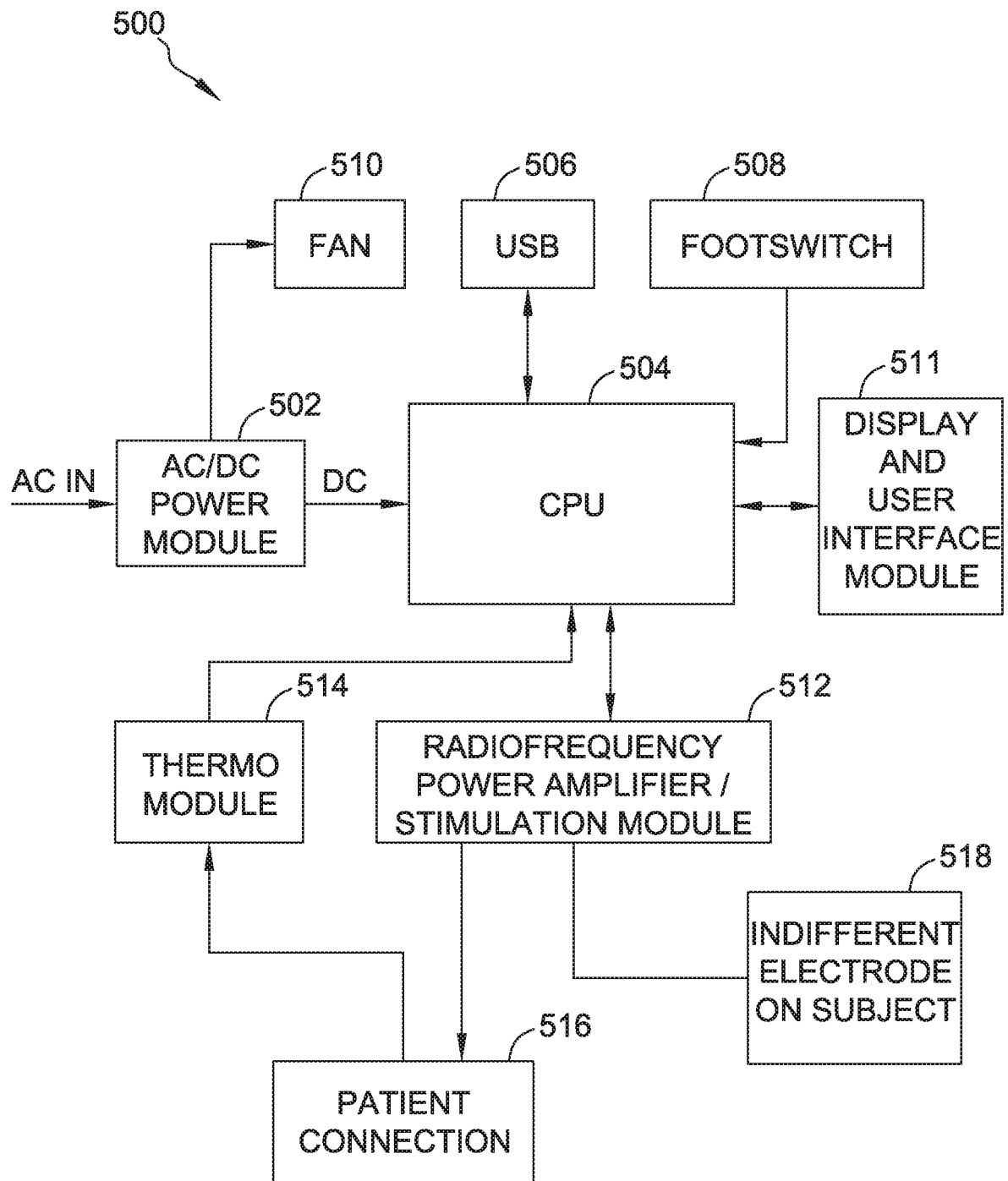


FIG. 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/038659

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61B5/00 A61B18/00 A61B17/00
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

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 2014/025069 A1 (HILL J P; WILLARD M R) 23 January 2014 (2014-01-23) paragraph [0074] - paragraph [0079]; figure 8	1-9
X	WO 2012/068471 A1 (BOSTON SCIENT SCIMED INC [US]; CROW LOREN M [US]; JENSON MARK L [US];) 24 May 2012 (2012-05-24) page 21, line 22 - page 22, line 15; figure 6	1-9
X	US 2014/303617 A1 (SHIMADA JIN [US]) 9 October 2014 (2014-10-09) paragraph [0095] - paragraph [0097]; figure 1	1-9
X	US 2014/200578 A1 (GROFF JOEL N [US] ET AL) 17 July 2014 (2014-07-17) paragraphs [0062], [0069]; figure 4	1-9



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

25 September 2017

Date of mailing of the international search report

04/10/2017

Name and mailing address of the ISA/

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Authorized officer

Cornelissen, P

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/038659

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.: 10-15
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:
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:
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2017/038659

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 2012068471 A1	24-05-2012

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US 2014200578 A1	17-07-2014	US 2014200578 A1	17-07-2014
		WO 2014110579 A1	17-07-2014
