Title: METHOD FOR TREATING A RENAL DISEASE OR DISORDER

Abstract:
METHOD FOR TREATING A RENAL DISEASE OR DISORDER

Related Application

This application claims priority from U.S. Provisional Patent Application Serial No. 60/932,229, filed May 30, 2007, the subject matter of which is incorporated herein by reference.

Technical Field

The present invention relates generally to renal neuromodulation, and more particularly to a method for treating a renal disease or disorder via an implantable neuromodulation device capable of delivering electric current to a desired vascular location.

Background of the Invention

The kidneys are a pair of organs that lie in the back of the abdomen on each side of the vertebral column. The kidneys play an important regulatory role in maintaining the homeostatic balance of the body. For example, the kidneys eliminate foreign chemicals from the body, regulate inorganic substances and extracellular fluid, and function as endocrine glands, secreting hormonal substances like renin and erythropoietin.

The main functions of the kidneys are maintaining the water balance of the body and controlling metabolic homeostasis. Healthy kidneys regulate the amount of fluid in the body by making urine more or less concentrated, thus either reabsorbing or excreting more fluid, respectively. Urine production in the kidneys is regulated in part through autoregulation, which involves reflexive changes in the diameters of the arterioles supplying the nephrons, thereby altering blood flow and filtration rates. Both hormonal and neural mechanisms can supplement or adjust the local responses.

The kidneys and ureters are innervated by the renal nerves. Most of the nerve fibers involved are sympathetic postganglionic fibers from the superior mesenteric ganglion. A renal nerve enters each kidney at the hilus and follows the branches of the renal artery to reach individual nephrons. Known functions of sympathetic innervation include: (1) regulation of renal blood flow and
pressure; (2) stimulation of renin release; and (3) direct stimulation of water and sodium ion resorption.

A variety of methods are currently used to treat kidney disease and conditions associated with kidney disease. For example, pharmacological compositions, such as FERRLECIT (iron gluconate) and VEROFER (iron sucrose), dialysis, and surgical intervention, such as kidney transplantation, are all used. Another method used to treat kidney disease and conditions associated with kidney disease involves electrostimulation of the renal nerves. Such electrostimulation methods, however, are often non-specific and offer only short-term symptomatic relief.

**Summary of the Invention**

In one aspect of the present invention, a method is provided for treating a renal disease or disorder. One step of the method includes determining the geometry of a desired vascular location where modulation of the sympathetic nervous system (SNS) is possible. Next, the geometry of an implantable neuromodulation device is adjusted to correspond to the geometry of the desired vascular location. The neuromodulation device is then implanted at the desired vascular location and electric current is delivered to the neuromodulation device to effect a change in the SNS.

In another aspect of the present invention, a method is provided for treating a renal disease or disorder. One step of the method includes determining the geometry of a desired vascular location where modulation of the SNS is possible. Next, an implantable neuromodulation device is provided. The neuromodulation device comprises an expandable support member having a main body portion for engaging a wall of a blood vessel proximate a renal vasculature, at least one electrode connected with the main body portion arranged to selectively deliver electric current to a desired location, and an insulative material attached to at least a portion of the main body portion for isolating blood flow through the vessel from the electric current delivered by the at least one electrode. The geometry of the implantable neuromodulation device is then adjusted to correspond to the geometry of the desired vascular location. Next, the neuromodulation device is implanted at
the desired vascular location. Electric current is then delivered to the
neuromodulation device to effect a change in the SNS.

**Brief Description of the Drawings**

The foregoing and other features of the present invention will become
apparent to those skilled in the art to which the present invention relates upon
reading the following description with reference to the accompanying drawings, in
which:

Fig. 1 is a process flowchart illustrating a method for treating a renal
disease or condition according to the present invention;

Fig. 2 is a perspective view of a neuromodulation device for insertion into a
blood vessel constructed in accordance with the present invention;

Fig. 3 is a schematic illustration of the autonomic nervous system showing
the sympathetic division and the projections of the sympathetic division;

Fig. 4 is an elevation view of the splanchnic nerves and celiac ganglia;

Fig. 5 is a schematic view illustrating the human renal anatomy;

Fig. 6 is a schematic view illustrating sympathetic innervation of the renal
anatomy;

Fig. 7A is a perspective view showing the neuromodulation device in Fig. 2
receiving electrical energy from a wireless energy delivery source;

Fig. 7B is a schematic sectional view taken along Line 7B-7B in Fig. 7A;

Fig. 8A is a perspective view showing an alternative embodiment of the
neuromodulation device shown in Fig. 2;

Fig. 8B is a schematic sectional view taken along Line 8B-8B in Fig. 8A;

Fig. 9A is a perspective view showing another alternative embodiment of
the neuromodulation device shown in Fig. 2;

Fig. 9B is a schematic sectional view taken along Line 9B-9B in Fig. 9A;

Fig. 10 is a perspective view showing an alternative embodiment of the
neuromodulation device in Fig. 2;

Fig. 11 is a perspective view showing another alternative embodiment of
the neuromodulation device in Fig. 2;
Fig. 12 is a perspective view showing another alternative embodiment of the neuromodulation device shown in Fig. 2;

Fig. 13 is a perspective view showing an alternative embodiment of the neuromodulation device shown in Fig. 12;

Fig. 14 is a perspective view showing another alternative embodiment of the neuromodulation device shown in Fig. 2;

Fig. 15 is a schematic view showing a guidewire extending through a femoral artery into the abdominal aorta;

Fig. 16 is a schematic view showing the neuromodulation device of Fig. 13 being delivered to the abdominal aorta proximate the renal vasculature;

Fig. 17 is a schematic view showing branch members being delivered to the abdominal aorta proximate the renal vasculature;

Fig. 18 is a schematic view showing the neuromodulation device of Fig. 2 implanted in the renal anatomy;

Fig. 19 is a schematic view showing branch members implanted in the renal vasculature;

Fig. 20 is a schematic view showing an alternative embodiment of the neuromodulation device in Fig. 2 implanted in the renal anatomy; and

Fig. 21 is a schematic view showing an alternative embodiment of the neuromodulation device in Fig. 2 placed extravascularly about a left renal artery.

**Detailed Description**

The present invention relates generally to renal neuromodulation, and more particularly to a method for treating a renal disease or disorder via an implantable neuromodulation device capable of delivering an electric current to a desired vascular location. As representative of the present invention, Fig. 1 illustrates a method 200 for treating a renal disease or disorder. As discussed in more detail below, the present invention provides a method 200 for treating a renal disease or disorder, such as renal hypertension. It will be appreciated, however, that other renal disease or disorders treatable by the method 200, such as those provided below are also within the scope of the present invention.
Unless otherwise defined, all technical terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the present invention pertains.

In the context of the present invention, the term “renal vasculature” refers to the kidneys and their associated anatomical structures, such as the renal arteries, the renal veins, and the ureters.

As used herein, the term “sympathetic nervous system” or “SNS” refers to the part of the autonomic nervous system originating in the thoracic and lumbar regions of the spinal cord that generally inhibits or opposes the physiological effects of the parasympathetic nervous system.

As used herein, the term “desired vascular location” refers to a desired anatomical location at which the present invention may be positioned. The desired vascular location can comprise a variety of anatomical locations, including intraluminal and extraluminal locations innervated by at least one nerve. For example, the desired vascular location can comprise an intravascular or extravascular location innervated by at least one nerve. Examples of desired vascular locations according to the present invention include, but are not limited to, the renal sinus, the renal arteries, the intraabdominal artery, the smaller arteries and arterioles of the kidneys, such as the segmental arteries, the lobar arteries, the interlobar artery, the arcuate arteries, the afferent arterioles, and the glomerulus, the left and right ureters, the renal ganglia, such as the celiac ganglia, the superior mesenteric ganglion, the left and right aorticorenal ganglia, the inferior mesenteric ganglion, and the efferent fibers emanating therefrom. Desired vascular locations contemplated by the present invention are also illustrated in Figs. 3-6 and Figs. 15-21, and are described in further detail below.

As used herein, the term “anastomosis” refers to a connection between two lumens that puts the lumens in fluid communication with each other. “Anastomosing” refers to the process of forming an anastomosis.

As used herein, the terms “renal disease” or “renal disorder” refer to any disease or disorder afflicting the renal vasculature and/or renal physiology. Renal disease may be marked by decline in kidney function over time (i.e., a chronic condition), as well as acute damage to the kidneys resulting in loss of renal
function. Renal disease can result from a primary pathology of the kidneys (e.g., injury to the glomerulus or tubule) or another organ (e.g., pancreas) that adversely affects the ability of the kidneys to perform biological functions (e.g., retain protein). Thus, renal disease can be the direct or indirect effect of disease.

Examples of a renal disease as a result or consequence of an indirect effect on the kidneys is kidney disease as a consequence of diabetes or systemic lupus. Other examples of renal disease include, but are not limited to, nephritis (acute and chronic), nephropathy, hyperfiltration, mild microalbuminuria, clinical albuminuria, kidney failure, polycystic kidney disease, chronic renal insufficiency, chronic or acute renal failure, end-stage renal disease, acute nephritic syndrome, analgesic nephropathy, atheroembolic renal disease, Goodpasture's syndrome, interstitial nephritis, kidney cancer, kidney infection, kidney stones, membranoproliferative glomerulonephritis (GN) I, membranoproliferative GN II, membranous nephropathy, necrotizing GN, nephrocalcinosis, post-streptococcal GN, reflux nephropathy, renal artery embolism, renal artery stenosis, renal papillary necrosis, renal tubular acidosis (types I and II), renal underperfusion, renal vein thrombosis, and disorders or diseases associated with renal disease, such as chronic or acute congestive heart failure and hypertension (e.g., chronic and acute hypertension).

As used herein, the term “renal excretion” refers to the removal of organic wastes from bodily fluids by the kidneys.

As used herein, the term “renal elimination” refers to the discharge of waste products via the kidneys and/or ureters.

As used herein, the term “homeostatic regulation” refers to the regulation or control of blood plasma volume and solute concentration by the kidneys. Examples of homeostatic regulation include: (1) regulation of blood volume and pressure by, for example, adjusting volume of water lost in the urine and releasing erythropoietin and renin; (2) regulating plasma ion concentrations (e.g., sodium, potassium, chloride ions, and calcium ion levels) by controlling the quantities lost in the urine and the synthesis of calcitrol; (3) stabilizing blood pH by controlling loss of hydrogen and bicarbonate ions in the urine; (4) conserving valuable
nutrients by preventing their excretion; and (5) assisting the liver with detoxification.

As used herein, the term “subject” refers to any warm-blooded organism including, but not limited to, human beings, pigs, rats, mice, dogs, goats, sheep, horses, monkeys, apes, rabbits, cattle, etc.

A brief discussion of the neurophysiology is provided to assist the reader with understanding the present invention. The ANS is a subsystem of the human nervous system that controls involuntary actions of the smooth muscles (blood vessels and digestive system), the heart and glands (Fig. 3). The ANS is divided into the SNS 32 and the PNS. The SNS 32 generally prepares the body for action by increasing heart rate, increasing blood pressure, and increasing metabolism. The PNS prepares the body for rest by lowering heart rate, lowering blood pressure, and stimulating digestion.

Several large sympathetic nerves and ganglia are formed by the neurons of the SNS 32 (Fig. 4). The greater splanchnic nerve (GSN) 34 is formed by efferent sympathetic neurons exiting the spinal cord from thoracic vertebral segment numbers 4 or 5 (T4 or T5) through thoracic vertebral segment numbers 9, 10 or 11 (T9, T10 or T11). The lesser splanchnic nerve (lesser SN) 36 is formed by preganglionic, sympathetic efferent fibers from T10 to T12. The least splanchnic nerve (least SN) 38 is formed by fibers from T12. The GSN 34 is typically present bilaterally in animals, including humans, with the other splanchnic nerves having a more variable pattern. The splanchnic nerves run along the anterior-lateral aspect of the vertebral bodies, pass out of the thorax, and enter the abdomen through the diaphragm 40. The splanchnic nerves run in proximity to the azygous veins (not shown). Once in the abdomen, neurons of the GSN 34 synapse with postganglionic neurons primarily in celiac ganglia 42. Some neurons of the GSN 34 pass through the celiac ganglia 42 and synapse in the adrenal medulla 44 (Fig. 6) (not shown in detail). Neurons of the lesser SN 36 (Fig. 4) and least SN 38 synapse with post-ganglionic neurons in the mesenteric ganglia, such as the superior mesenteric ganglion 46 and the inferior mesenteric ganglion 48 (Fig. 6).

Postganglionic neurons, arising from the celiac ganglia 42 (Fig. 4) that synapse with the GSN 34, innervate primarily the upper digestive system,
including the stomach, pylorus, duodenum, pancreas and liver. In addition, blood vessels and adipose tissue of the abdomen are innervated by neurons arising from the celiac ganglia 42 and GSN 34. Postganglionic neurons of the mesenteric ganglia, supplied by preganglionic neurons of the lesser and least splanchnic nerve 36 and 38, innervate primarily the lower intestine, colon, rectum, kidneys, bladder, and sexual organs, and the blood vessels that supply these organs and tissues.

Fig. 5 illustrates the renal vasculature 30, including the ureters 68 and 70. The left and right kidneys 50 and 52 are located lateral to the vertebral column between the last thoracic and third lumbar vertebrae on each side. The superior surface of the right kidney 52 is situated inferior to the superior surface of the left kidney 50. The position of the kidneys 50 and 52 in the abdominal cavity is maintained by the overlying peritoneum, contact with adjacent visceral organs, and supporting connective tissues. Each of the kidneys 50 and 52 is protected and stabilized by three concentric layers of connective tissue (i.e., the renal capsule, the adipose capsule, and the renal fascia).

The kidneys 50 and 52 receive 20-25% of the total cardiac output. In normal individuals, about 1200 mL of blood flows through the kidneys 50 and 52 each minute. Each of the kidneys 50 and 52 receives blood from left and right renal arteries 54 and 56, respectively, that originate along the lateral surface of the abdominal aorta 58 near the level of the superior mesenteric artery 60 (Fig. 4). For the purposes of the present invention and for ease of reference, the left and right renal arteries 54 and 56 may each be segmented into proximal 61, medial 63, and distal 65 portions (Fig. 5).

As the renal arteries 54 and 56 enter the renal sinuses (not shown), they branch into the segmental arteries (not shown). The segmental arteries further divide into a series of interlobular arteries (not shown) that radiate outward, penetrating the renal capsule and extending through the renal columns (not shown) between the renal pyramids (not shown). The interlobular arteries supply blood to the arcuate arteries (not shown) that parallel the boundary between the cortex (not shown) and medulla (not shown) of the kidneys 50 and 52. Each arcuate artery
gives rise to a number of interlobular arteries supplying portions of the adjacent renal lobe.

Numerous afferent arterioles (not shown) branch from each interlobular artery to supply individual nephrons (not shown). From the nephrons, blood enters a network of venules (not shown) and small veins (not shown) that converge on the interlobular veins (not shown). In a mirror image of the arterial distribution, the interlobular veins deliver blood to arcuate veins (not shown) that empty into further interlobular veins. The interlobular veins merge to form the renal veins 62 and 64, which drain into the inferior vena cava 66.

Fig. 6 illustrates sympathetic innervation of the renal vasculature 30. The kidneys 50 and 52 are innervated by renal nerves 72. Most of the nerves 72 involved are sympathetic postganglionic fibers from the superior mesenteric ganglion 46. Renal nerves 72 enter each of the kidneys 50 and 52 at the hilum 74 and follow the branches of the renal arteries 54 and 56 to reach individual nephrons. Other renal ganglia, such as the celiac ganglia 42, the superior mesenteric ganglion 46, the left and right aorticorenal ganglia 76 and 78, and the inferior mesenteric ganglion 48 also innervate the renal vasculature 30. Known functions of sympathetic innervation include: (1) regulation of renal blood flow and pressure; (2) stimulation of renin release; and (3) direct stimulation of water and sodium ion reabsorption.

To address the problems of renal disease and diseases or conditions associated with renal disease, the present invention provides a method 200 for renal neuromodulation to treat a renal disease or disorder. More particularly, the present invention recognizes that subjects have different vascular geometries, and that a given implantable medical device, such as an intravascular stent may not be appropriate for a given subject in view of such anatomical differences. The method 200 of the present invention overcomes the problems associated with varying vascular geometries by providing an implantable neuromodulation device 10 having a tailored geometry that corresponds to the vascular geometry of an individual subject. The present invention thus provides a tailored approach to modulating different facets of renal function including, for example, renal excretion, renal elimination, and homeostatic regulation.
Referring to Fig. 1, a method 200 for treating a renal disease or disorder is illustrated. At 202, the geometry of a desired vascular location where modulation of the SNS is possible is first determined. Suitable vascular locations can include, for example, an intravascular location adjacent to, or innervated by, at least one nerve associated with the renal ganglia (e.g., the celiac ganglion, the superior mesenteric ganglion, the left and right aorticorenal ganglia, the inferior mesenteric ganglion, and the efferent fibers emanating therefrom).

To determine the geometry of the desired vascular location, any one or combination of known imaging techniques can be used. For example, two-, three-, and four-dimensional imaging modalities such as MRI (e.g., MR angiography), CT (e.g., CT angiography), ultrasound (e.g., duplex Doppler), X-ray, and digital fluoroscopy may be used to determine the geometry of the desired vascular location. Using one or combination of known imaging techniques, different geometric parameters of the desired vascular location, such as vessel length, perimeter, area, blood flow, transmural pressure, curvature, and intraluminal diameter may be readily determined. For example, where the desired vascular location comprises a portion of the abdominal aorta 58 and a portion of the left and right renal arteries 54 and 56, MR angiography may be used to determine the vessel length and intraluminal diameters of the abdominal aorta and the renal arteries.

At 204, the geometry of an implantable neuromodulation device 10 is adjusted to correspond to the geometry of the desired vascular location. As shown in Fig. 1, for example, the neuromodulation device 10 can comprise an expandable support member 12 for engaging a wall of a blood vessel and for modulating renal function. As used herein, the term “modulate” or “modulating” refers to causing a change in neuronal activity, chemistry, and/or metabolism. The change can refer to an increase, decrease, or even a change in a pattern of neuronal activity. For example, efferent nerve activity and/or afferent nerve activity of the SNS, PNS, PNS and SNS, or somatic nervous system can be modulated by the present invention. The term may refer to either excitatory or inhibitory stimulation, or a combination thereof, and may be at least electrical, biological, magnetic, optical or chemical, or a combination of two or more of these. The term “modulate” can also
be used to refer to a masking, altering, overriding, or restoring of neuronal activity. It will be appreciated that the same or different apparatus 10 can be used to modulate neuronal activity of a first nerve in one manner and the neuronal activity of a second nerve in a different manner.

As shown in Fig. 2, the expandable support member 12 includes oppositely disposed first and second end portions 24 and 26 and a main body portion 14 extending between the end portions. The structure of the expandable support member 12 may be a mesh, a zigzag wire, a spiral wire, an expandable stent, or other similar configuration that allows the expandable support member to be collapsed and expanded. The expandable support member 12 can be comprised of a material having a high modulus of elasticity, including, for example, cobalt-nickel alloys (e.g., Elgiloy), titanium, nickel-titanium alloys (e.g., Nitinol), cobalt-chromium alloys (e.g., Stellite), nickel-cobalt-chromium-molybdenum alloys (e.g., MP35N), graphite, ceramic, stainless steel, and hardened plastics. The expandable support member 12 may also be made of a radio-opaque material or include radio-opaque markers to facilitate fluoroscopic visualization.

The flexible and expandable properties of the expandable support member 12 facilitate percutaneous delivery of the expandable support member, while also allowing the expandable support member to conform to a portion of a blood vessel. An expanded configuration of the expandable support member 12 is shown in Fig. 2. In the expanded configuration, the expandable support member 12 has a circular cross-sectional shape for conforming to the circular cross-sectional shape of the blood vessel lumen. By conforming to the shape of the blood vessel lumen, the expanded configuration of the expandable support member 12 facilitates movement of the blood flow therethrough while also maintaining lumen patency.

At least one constraining band 28 may be placed around the circumference of the expandable support member 12 to maintain the expandable support member in the collapsed configuration. As shown in Fig. 16, the constraining bands 28 may comprise sutures, for example, and may be placed around the circumference of the expandable support member 12 as needed. Removal of the constraining bands 28 allows the expandable support member 12 to self-expand and obtain the
expanded configuration. Where the constraining bands 28 comprise sutures, for example, the sutures may be manually broken or, alternatively, broken by the radial force generated when the expandable support member 12 self-expands. It will be appreciated that the constraining bands 28 may comprise any other type of material capable of being selectively modified. For example, the constraining bands 28 may be made of a shape memory alloy, such as Nitinol, which can be selectively modified (i.e., expanded) by delivering energy (e.g., thermal energy) to allow the expandable support member 12 to obtain the expanded configuration.

The expandable support member 12 (Fig. 2) also includes at least one fenestration 20 and at least one branch member 22. As shown in Fig. 2, and more clearly in Fig. 13, the fenestrations 20 include a hole or opening disposed about the main body portion 14 of the expandable support member 12. Fig. 2 illustrates an expandable support member 12 having two fenestrations 20; however, it will be appreciated that the expandable support member may include any number of fenestrations disposed about the main body portion 14.

As shown in Fig. 2, the expandable support member 12 also includes two branch members 22. The branch members 22 are constructed in an identical or substantially identical fashion as the main body portion 14 of the expandable support member 12, and include first and second end portions 23 and 25. The first end portion 23 of each of the branch members 22 is anastomosed with the fenestrations 20 such that the lumen of each of the branch members is in fluid communication with the lumen of the main body portion 14. As described in more detail below, the first end portion 23 of each of the branch members 22 may be anastomosed with the fenestrations 20 using any one or combination of techniques known in the art. Means for anastomosing the first end portion 23 of each of the branch members 22 to the fenestrations include 20, but are not limited to, sutures, clips, staples, pins, adhesives, and the like. Although the expandable support member 12 of Fig. 2 is shown with two branch members 22, it should be appreciated that any number of branch members may be included with the expandable support member.

The expandable support member 12 also includes at least one electrode 16 for delivering an electric current to a desired vascular location. As shown in
Fig. 2, the electrodes 16 have a flat, disc-like shape and are radially disposed about the circumference of the expandable support member 12 in a multi-electrode array configuration. It will be appreciated, however, that the electrodes 16 may have any shape and size, including, for example, a triangular shape, a rectangular shape, an ovoid shape, and/or a band-like shape (e.g., a split band configuration), and are not limited to the shapes and sizes illustrated in Fig. 2. The electrodes 16 may be configured so that the expandable support member 12 has a unipolar construction (Fig. 7A) using the surround tissue as ground or, alternatively, a bipolar construction using leads connected to either end of the expandable support member (Fig. 8A). The electrodes 16 may be made of any material capable of conducting an electrical current, such as platinum, platinum-iridium, or the like.

As shown in Fig. 2, the electrodes 16 can extend around only a portion or the entire circumference of the expandable support member 12 in a radial fashion. Alternatively, the electrodes 16 may extend around only a portion or the entire circumference of the expandable support member 12 in a sinusoidal or helical fashion (Fig. 8A). The entire length of the expandable support member 12 may be covered with the electrodes 16 or, alternatively, only a portion of the expandable support member, such as the first end portion 24 (Fig. 10), may be covered with the electrodes. Additionally, it will be appreciated that the electrodes 16 may extend around only the main body portion 14 or, alternatively, only around the branch members 22 (Fig. 11).

To facilitate focal delivery of electrical energy to a desired vascular location, the electrodes 16 may wrap around the expandable support member 12 any number of times to establish a desired electrode contact and coverage. Additionally or optionally, the entire surface area of the electrodes 16 may be conductive or, alternatively, only a portion of the surface area of the electrodes may be conductive. By modifying the conductivity of the surface of the electrodes 16, the surface area of the electrodes that contact the blood vessel wall may be selectively modified to facilitate focal delivery of electrical energy to the desired vascular location.

Electrical energy can be delivered to the electrodes 16 using a variety of internal, passive, or active energy sources 80 (Figs. 7A-9B). The energy source 80
may include, for example, radio frequency (RF) energy, X-ray energy, microwave energy, acoustic or ultrasound energy such as focused ultrasound or high intensity focused ultrasound energy, light energy, electric field energy, magnetic field energy, combinations of the same, or the like. As shown in Fig. 8A, for example, an energy source 80 may be directly coupled to the neuromodulation device 10 using an electrical lead 82. The electrical lead 82 may be disposed in an adjacent blood vessel, such as the inferior vena cava 66, and travel down the length of the inferior vena cava to a remote entry site (not shown). Alternatively, as shown in Figs. 9A-B, electrical energy may be supplied to the electrodes 16 via a turbine-like mechanism 84 operatively disposed in the lumen of the expandable support member 12. As blood flows through the lumen of the expandable support member 12, the turbine mechanism 84 generates electrical energy which may then be delivered to the electrodes 16. Further, the energy source 80 may be wirelessly coupled to the neuromodulation device 10 as shown in Fig. 7A.

It will be appreciated that the energy source 80 can include a rechargeable battery (not shown) that is operably coupled to the apparatus 10. For example, an external charger (not shown) can be inductively coupled to a charging circuit (not shown) that is operably coupled to the apparatus 10 to recharge the battery. The external charger can include a charging coil energizable to create an electromagnetic field that in turn induces current in a corresponding coil within the charging circuit. The coil may be mounted to a waist pack, wearable skin-contacting/adhering patch, purse, backpack, or wheelchair cushion, for example, so that it can be carried by the patient in sufficient proximity to the charging circuit. Alternatively, the coil may be positioned within a pad positionable on a subject’s mattress, allowing for charging of the battery while the subject rests.

Electrical energy can be delivered to the electrodes 16 continuously, periodically, episodically, or a combination thereof. For example, electrical energy can be delivered in a unipolar, bipolar, and/or multipolar sequence or, alternatively, via a sequential wave, charge-balanced biphase square wave, sine wave, or any combination thereof. Electrical energy can be delivered to all the electrodes 16 at once or, alternatively, to only a select number of desired electrodes. The particular voltage, current, and frequency delivered to the electrodes 16 may be varied as
needed. For example, electrical energy can be delivered to the electrodes 16 at a constant voltage (e.g., at about 0.1 v to about 25 v), at a constant current (e.g., at about 25 microamperes to about 50 milliamperes), at a constant frequency (e.g., at about 5 Hz to about 10,000 Hz), and at a constant pulse-width (e.g., at about 50 μsec to about 10,000 μsec).

Delivery of electrical energy to a select number of electrodes 16 may be accomplished via a controller (not shown), for example, operably attached to the neuromodulation device 10. The controller may comprise an electrical device which operates like a router by selectively controlling delivery of electrical energy to the electrodes 16. For example, the controller may vary the frequency or frequencies of the electrical energy being delivered to the electrodes 16. By selectively controlling delivery of electrical energy to the electrodes 16, the controller can facilitate focal delivery of electrical energy to a desired vascular location.

It should be appreciated that means other than electrical energy, such as chemical or biological means, may also be used for renal neuromodulation. For example, the neuromodulation device 10 may include at least one pharmacological agent for eluting into the vascular tissue and/or blood stream. The pharmacological agent may be capable of preventing a variety of pathological conditions including, but not limited to, hypertension, hypotension, anemia, thrombosis, stenosis and inflammation. Accordingly, the pharmacological agent may include at least one of a diuretic agent, an anti-anemia agent, an anti-hypertensive, an anti-hypotensive agent, an anticoagulant, an antioxidant, a fibrinolytic, a steroid, an anti-apoptotic agent, and an anti-inflammatory agent.

Another example of a pharmacological agent includes Botulinum toxin (e.g., BOTOX).

Optionally or additionally, the pharmacological agent may be capable of treating or preventing other diseases or disease processes such as microbial infections. In these instances, the pharmacological agent may include an antimicrobial agent and/or a biological agent such as a cell, peptide, or nucleic acid. The pharmacological agent can be simply linked to the surface of the neuromodulation device 10, embedded and released from within polymer
materials, such as a polymer matrix, or surrounded by and released through a carrier.

Referring again to Fig. 2, the expandable support member 12 additionally comprises an insulative material 18 for isolating blood flow through the vessel from the electric current. More particularly, the insulative material 18 serves as an electrical insulator, separating electrical energy from blood flow and facilitating delivery of electrical energy to the vessel wall. The insulative material 18 is disposed radially inward of the electrodes 16 and extends along the entire length of the expandable support member 12. Alternatively, the insulative material 18 may be attached to select portions of the expandable support member 12, such as only the second end portion 26 and part of the main body portion 14. The insulative material 18 may be disposed between the electrodes 16 and the expandable support member 12 (Fig. 8B) or, alternatively, disposed about the lumen of the expandable support member (Figs. 7B and 9B). The insulative material 18 generally has a low electrical conductivity and a non-thrombogenic surface. The insulative material 18 can include materials such as PTFE, ePTFE, silicone, silicone-based materials, and the like.

In addition to the insulative layer 18, at least a portion of the expandable support member 12 may optionally include a layer (not shown) of biocompatible material. The layer of biocompatible material may be synthetic such as DACRON (Invista, Wichita, KS), GORE-TEX (W. L. Gore & Associates, Flagstaff, AZ), woven velour, polyurethane, or heparin-coated fabric. Alternatively, the layer of biocompatible material may be a biological material such as bovine or equine pericardium, peritoneal tissue, an allograft, a homograft, patient graft, or a cell-seeded tissue. The biocompatible layer can cover either the luminal surface of the expandable support member 12, the non-luminal surface of the expandable support member, or can be wrapped around both the luminal and non-luminal surfaces. The biocompatible layer may be attached around the entire circumference of the expandable support member 12 or, alternatively, may be attached in pieces or interrupted sections to allow the expandable support member to more easily expand and contract.
The apparatus 10 can be part of an open- or closed-loop system. In an open-loop system, for example, a physician or subject may, at any time, manually or by the use of pumps, motorized elements, etc. adjust treatment parameters such as pulse amplitude, pulse width, pulse frequency, or duty cycle. Alternatively, in a closed-loop system, electrical parameters may be automatically adjusted in response to a sensed symptom or a related symptom indicative of the extent of the renal disease being treated. In a closed-loop feedback system, a sensor 108 (Fig. 7A) that senses a condition (e.g., a metabolic parameter of interest) of the body can be utilized. More detailed descriptions of sensors 108 that may be employed in a closed-loop system, as well as other examples of sensors and feedback control techniques that may be employed are disclosed in U.S. Patent No. 5,716,377, the entirety of which is hereby incorporated by reference.

Although described in more detail below, it should be appreciated that incorporating the apparatus 10 as part of a closed-loop system can include placing the apparatus in a blood vessel adjacent a desired location, detecting a bodily activity associated with a renal disease, and then activating the apparatus to apply electric current to the desired location in response to the detected bodily activity. Such bodily activity can include any characteristic or function of the body, such as renal blood flow or renal volume, urine output, urine chemistry, urine osmolarity, plasma renin, plasma angiotensin, urine pH, specific gravity, urine protein content, urine blood content, urine ketone content, respiratory function (e.g., respiratory rate), body temperature, blood pressure, metabolic activity such as fluid glucose levels, hormone levels, enzyme or enzyme byproduct levels, and/or nitrogen, oxygen and/or carbon dioxide levels, body temperature, cerebral blood flow, pH levels (e.g., in blood, tissue, and other bodily fluids), galvanic skin responses (e.g., perspiration), electrocardiogram, muscle tone in the diaphragm and other muscles, electroencephalogram, nerve action potential, body movement, response to external stimulation, speech, motor activity, ocular activity, cognitive function, and the like.

It should be appreciated that an override mechanism (not shown) for overriding a closed-loop system can also be included as part of the present invention. For example, where a patient is diagnosed with congestive heart failure,
the override mechanism could be used to override the closed-loop system and permit diuresis of the patient.

Another embodiment of the neuromodulation device is illustrated in Fig. 12, the neuromodulation device 10, is identical to the neuromodulation device 10 illustrated in Fig. 2, except where as described below. In Fig. 12, structures that are identical as structures in Fig. 2 use the same reference numbers, whereas structures that are similar but not identical carry the suffix “a”.

As shown in Fig. 12, the neuromodulation device 10 comprises an expandable support member 12, having a main body portion 14, for engaging a wall of a blood vessel proximate a renal vasculature 30. The expandable support member 12 includes at least one electrode 16 arranged to selectively deliver electric current to a desired vascular location where modulation of the SNS is effective to alter renal function. Additionally, the expandable support member 12 includes an insulative material 18 attached to at least a portion of the main body portion 14. As discussed above, the insulative material 18 is for isolating blood flow through the vessel from the electric current delivered by the electrodes 16. The expandable support member 12 may also include at least one fenestration 20 as illustrated in Fig. 13.

Another embodiment of the neuromodulation device is illustrated in Fig. 14. In Fig. 14, the neuromodulation device 10, is identical to the neuromodulation device 10 illustrated in Fig. 12, except where as described below. In Fig. 14, structures that are identical as structures in Fig. 12 use the same reference numbers, whereas structures that are similar but not identical carry the suffix “b”.

As shown in Fig. 14, the neuromodulation device 10 comprises an expandable support member 12, having a main body portion 14, for engaging a wall of a blood vessel proximate a renal vasculature 30. The expandable support member 12 includes at least one electrode 16 arranged to selectively deliver electric current to a desired vascular location where modulation of the SNS is effective to alter renal function. Additionally, the expandable support member 12 includes at least one wireless module 86 capable of receiving electrical energy for delivery to the electrodes 16. It should be appreciated that the neuromodulation
device 10, shown in Fig. 14 may include other components, such as
fenestrations 20 and branch members 22.

The wireless module 86 may be operably coupled to the expandable
support member 12 as shown in Fig. 14. The wireless module 86 may comprise
an electrical device which operates like a router by selectively controlling delivery
of electrical energy to the electrodes 16. For example, the wireless module 86 may
vary the frequency or frequencies of the electrical energy being delivered to the
electrodes 16. By selectively controlling delivery of electrical energy to the
electrodes 16, the wireless module 86 can facilitate focal delivery of electrical
energy to a desired vascular location. Alternatively, the wireless module 86 may
passively distribute electrical energy to the electrodes 16.

The geometry of the neuromodulation device 10 can be adjusted at 204
using known stent fabrication methods and materials based on a particular
subject’s vessel geometry. For example, female subjects typically have smaller
vessel geometries when compared to male subjects. Additionally, diabetic subjects
may have smaller vessel geometries than non-diabetic subjects. Where the
neuromodulation device 10 of Fig. 2 is to be implanted at a desired vascular
location in a female subject, for example, the diameter of the main body portion 14
of the expandable support member 12 and the branch members 22 may be adjusted
(e.g., reduced) to correspond to the geometry of the abdominal aorta 58 and renal
arteries 54 and 56, respectively.

After adjusting the geometry of the neuromodulation device 10, the
neuromodulation device is implanted at the desired vascular location at 206. The
neuromodulation device 10 is implanted using a minimally invasive, percutaneous,
or endovascular approach. It should be appreciated, however, that a minimally
invasive surgical approach may also be used. For purposes of illustration only, the
present invention is described with reference to the neuromodulation device 10
being positioned in the renal arteries 54 and 56 and in the abdominal aorta 58
proximate the renal arteries. It will be appreciated, however, that the
neuromodulation device 10 may additionally or optionally be placed at other
desired vascular locations, such as in the renal veins 62 and 64, the inferior vena
cava 66 proximate the renal veins, the superior mesenteric artery 60, and/or the celiac artery 88 (Fig. 4).

Percutaneous placement of the neuromodulation device 10 starts by accessing a bodily vessel with a delivery device. For instance, a first guidewire 90 (Fig. 15) may be introduced into the vasculature via a vascular opening or incision (not shown). Vascular access may be through a peripheral arterial access site (not shown), such as a left femoral artery 92. The first guidewire 90 is inserted through the incision into the left femoral artery 92 in an antegrade direction. Alternatively, the first guidewire 90 may be inserted into the brachiocephalic artery (not shown) from an incision in the left subclavian artery (not shown) or left brachial artery (not shown) in a retrograde direction, or in a retrograde direction through the right subclavian artery (not shown), and then advanced toward the abdominal aorta 58. The first guidewire 90 is then urged into the abdominal aorta 58 proximate the renal arteries 54 and 56 as shown in Fig. 15.

Next, the main body portion 14 of the expandable support member 12 is placed in a first delivery catheter 94 in a collapsed configuration and securely attached to a proximal end (not shown) of the first guidewire 90. The first delivery catheter 94 is then advanced over the first guidewire 90 as shown in Fig. 17. The first delivery catheter 94 is advanced until the first delivery catheter is suitably positioned in the abdominal aorta 58 proximate the renal arteries 54 and 56. In particular, the main body portion 14 is positioned such that each of the fenestrations 20 is adjacent the ostium of each of the left and right renal arteries 54 and 56. Additionally, the main body portion 14 is positioned such that at least a portion of the main body portion is positioned substantially adjacent a desired target. For example, a portion of the main body portion 14 having a focal arrangement of electrodes 16 is positioned substantially adjacent the superior mesenteric ganglion 46 (Fig. 18).

Once the main body portion 14 of the expandable support member 12 is appropriately positioned in the abdominal aorta 58 proximate the renal arteries 54 and 56, the first delivery catheter 94 is removed and the constraining bands 28 are progressively released (i.e., broken) by the radial force generated by the self-expanding main body portion. When all of the constraining bands 28 have been
released, the main body portion 14 obtains the expanded configuration and is securely positioned in the abdominal aorta 58 proximate the renal arteries 54 and 56. With the main body portion 14 securely positioned in the abdominal aorta 58, the first guidewire 90 is then removed from the vasculature.

As shown in Fig. 17, second and third guidewires 96 and 98 are then inserted into the left femoral artery 92 and advanced in an antegrade direction. The second and third guidewires 96 and 98 are advanced so that the second and third guidewires respectively extend into the left and right renal arteries 54 and 56. Next, first and second branch members 100 and 102 are respectively placed in second and third delivery catheters 104 and 106 in a collapsed configuration and securely attached to the proximal ends (not shown) of the second and third guidewires 96 and 98. The second and third delivery catheters 104 and 106 are then respectively advanced in an antegrade direction over the second and third guidewires 96 and 98 as shown in Fig. 17. The second and third delivery catheters 104 and 106 are next respectively advanced through the lumen of the main body portion 14, through the fenestrations 20, and into the left and right renal arteries 54 and 56.

After delivery to the left and right renal arteries 54 and 56, the first and second branch members 100 and 102 are positioned such that each branch member is substantially adjacent a desired vascular location. As shown in Fig. 18, for example, the first and second branch members 100 and 102 are positioned so that the electrodes 16 of each of the branch members is located in the proximal portion 61 of each of the left and right renal arteries 54 and 56. Consequently, the electrodes 16 of each of the first and second branch members 100 and 102 are positioned substantially adjacent the left and right aortic renal ganglion 76 and 78, respectively. It should be appreciated that the arrangement of the electrodes 16 on each the branch members 22 may be varied to selectively deliver electrical energy to different portions of the renal arteries 54 and 56. For example, the electrodes 16 of the branch members 22 may be arranged so that electrical energy can be delivered to the medial 63 and/or distal portion 65 of each of the renal arteries 54 and 56 and thus deliver electrical energy to select renal nerves 72.
Once the first and second branch members 100 and 102 are appropriately positioned, the second and third delivery catheters 104 and 106 are removed and the constraining bands 28 are progressively released (i.e., broken) by the radial force generated by the self-expanding branch members. When all of the constraining bands 28 have been released, the first and second branch members 100 and 102 each obtain the expanded configuration and are securely positioned in the left and right renal arteries 54 and 56, respectively.

With the first and second branch members 100 and 102 respectively positioned in the left and right renal arteries 54 and 56, the first end portion 23 of each of the branch members is anastomosed with the corresponding fenestration 20 using, for example, sutures or ties (Fig. 18). The first and second branch members 100 and 102 are securely anastomosed with the fenestrations 20 such that the lumen of each of the branch members is in fluid communication with the lumen of the main body portion 14. It will be appreciated that other methods known in the art may be used to securely anastomose the first and second branch members 100 and 102 with the fenestrations 20. Examples of such methods are disclosed in U.S. Pat. No. 6,827,735 and U.S. Pat. Pub. No. 2006/0247761, each of which is hereby incorporated by reference in its entirety.

After the first and second branch members 100 and 102 are positioned in the left and right arteries 54 and 56, respectively, the second and third guidewires 96 and 98 are removed from the vasculature. Next, electrical energy, such as RF energy, may be delivered to the neuromodulation device 10 via a wirelessly coupled energy source 80 as shown in Fig. 18. As electrical energy is delivered to the neuromodulation device 10, the electrodes 16 conduct the electrical energy to the vascular wall at the desired vascular locations and thereby cause nerves associated with the desired vascular locations to fire action potentials. Electrical energy delivered to the electrodes 16 on the main body portion 14, for example, causes the superior mesenteric ganglion 46 to fire action potentials. The action potentials are then relayed to efferent nerve fibers, which emanate from the superior mesenteric ganglion 46 and innervate the efferent and afferent arterioles (not shown) of the kidneys 50 and 52.
Depending upon the desired neuromodulatory effect, electrical energy may be delivered to the electrodes 16 so that the efferent and/or afferent arterioles are either activated, inhibited, or alternately activated and inhibited. For example, electrical energy may be delivered to the electrodes 16 to cause constriction of the efferent arterioles which, in turn, may increase renal filtration and urine production. Alternatively, electrical energy may be delivered to the electrodes 16 to cause constriction of the afferent arterioles and thereby reduce renal filtration and urine production. Further, electrical energy may be delivered to the electrodes 16 to cause constriction of the efferent arterioles while alternately reducing or inhibiting constriction of the afferent arterioles and, thus, increase renal filtration and urine production.

Additionally or optionally, electrical energy may be delivered to the electrodes 16 to modulate the renin-angiotensin-aldosterone system (RAAS). The RAAS regulates renal vasomotor activity, maintains optimal salt and water homeostasis, and controls tissue growth in the kidneys 50 and 52. RAAS function is controlled by the SNS and, in particular, SNS modulation of juxtaglomerular apparatus (JGA) cells. The JGA cells form part of the wall of the afferent arterioles and secrete renin in response to various stimuli. In the kidneys 50 and 52, renin converts angiotensin to angiotensin I, which is then converted to angiotensin II by angiotensin converting enzyme in the lungs (not shown). Angiotensin II in turn causes water retention by two mechanisms: directly acting on tubules (not shown) to promote sodium and water reabsorption; and indirectly stimulating aldosterone secretion in the adrenal cortex (not shown).

Pathologic consequences can result from overactivity of the RAAS, thus involving the RAAS in the pathophysiology of kidney disease. An activated RAAS promotes both systemic and glomerular capillary hypertension, which can induce hemodynamic injury to the vascular endothelium and glomerulus. Dysfunction of the RAAS is also implicated in congestive heart failure and chronic renal failure.

Accordingly, electrical energy may be delivered to the electrodes 16 to effect a change in the RAAS. As described below, delivering electrical energy to the electrodes 16 may in turn alter renal function and thus be useful for treating
conditions related to or caused by renal dysfunction, such as hypertension, for example. Electrical energy can be delivered to the electrodes 16 to decrease or inhibit nerve conduction from the superior mesenteric ganglion 46 to select efferent nerve fibers. A decrease or inhibition of nerve conduction from the superior mesenteric ganglion 46 will decrease or inhibit activity of the JGA cells and, thus, decrease or inhibit renin production. As a result of a decrease in renin production, the RAAS will be altered and thereby lead to a decrease in blood pressure. It will be appreciated that modulating the SNS, and thus altering the RAAS, may be useful for treating not only hypertension, but also any number of other renal diseases or conditions associated therewith, such as congestive heart failure, chronic renal failure, and the like.

During delivery of electrical energy to the neuromodulation device 10, at least one metabolic parameter of interest, such as blood-sodium content, may be measured via a sensor 108 (Fig. 7A). The sensor 108 may comprise any suitable device that measures or monitors a parameter indicative of the need to modify the activity of the neuromodulation device 10. For example, the sensor 108 may comprise a physiologic transducer or gauge that measures blood pressure (systolic, diastolic, average or pulse pressure), blood volumetric flow rate, blood flow velocity, blood pH, O₂ or CO₂ content, nitrogen content, hemodynamic factors (e.g., renin/angiotensin, blood glucose, inflammatory mediators, tissue factors, etc.), mixed venous oxygen saturation (SVO₂), vasoactivity, nerve activity, and tissue activity or composition. The sensor 108 may be separate from the neuromodulation device 10 or combined therewith (Fig. 7A).

The sensor 108 may also be positioned in/on a blood vessel and/or organ, such as in a chamber of the heart (not shown), or in/on a major artery, such as the abdominal aorta 58, such that the parameter of interest may be readily ascertained. It will be appreciated that the sensor 108 can also be used to detect various urine-associated parameters of interest, such as urine output, urine chemistry, urine osmolality, urine pH, urine protein content, urine blood content, and urine ketone content. Additionally, it will be appreciated that the sensor 108 may be used to detect a metabolic parameter of interest associated with a renal disease or disorder.
Examples of sensors that may be used to detect the parameters are disclosed in U.S. Patent Application Ser. No. 12/016,115.

An electrical stimulus regimen comprising a desired temporal and spatial distribution of electrical energy to a desired vascular location may be selected to promote long-term efficacy of the present invention. It is theorized that uninterrupted or otherwise unchanging delivery of electrical energy to a desired vascular location may result in associated nerves becoming less responsive over time, thereby diminishing the long-term effectiveness of the therapy. Therefore, the electrical stimulus regimen may be selected to activate, deactivate, or otherwise modulate the neuromodulation device 10 in such a way that therapeutic efficacy is maintained for a desired period of time.

In addition to maintaining therapeutic efficacy over time, the electrical stimulus regimen may be selected to reduce the power requirement/consumption of the present invention. For example, the electrical stimulus regimen may dictate that the neuromodulation device 10 be initially activated at a relatively higher energy and/or power level, and then subsequently activated at a relatively lower energy and/or power level. The first level attains the desired initial therapeutic effect, and the second (lower) level sustains the desired therapeutic effect long term. By reducing the energy and/or power levels after the desired therapeutic effect is initially attained, the energy required or consumed by the neuromodulation device 10 is also reduced long-term.

It should be appreciated that unwanted collateral stimulation of adjacent tissues may be limited by creating localized cells or electrical fields (i.e., by limiting the electrical field beyond a desired vascular location). Localized cells may be created by, for example, spacing the electrodes 16 very close together or biasing the electrical field with conductors (not shown) and/or magnetic fields. For example, electrical fields may be localized or shaped by using electrodes 16 with different geometries, by using one or more multiple electrodes, and/or by modifying the frequency, pulse-width, voltage, stimulation waveforms, paired pulses, sequential pulses, and/or combinations thereof.

It should also be appreciated that more than one neuromodulation device 10 may be used to modulate the SNS. For example, it may be desirable to modulate
the celiac ganglia 42 via an electrical field by placing one neuromodulation device 10 in the abdominal aorta 58 proximate the renal arteries 54 and 56 and another neuromodulation device in the inferior vena cava 66 proximate the renal veins 62 and 64. With this arrangement, the electrical field created between the two neuromodulation devices 10 may be used to modulate SNS activity at the celiac ganglia 42. As shown in Fig. 19, it will be further appreciated that two branch members 22 can be respectively placed in the left and right renal arteries 54 and 56.

Although the above method is described in terms of modulating the SNS to treat a renal disease, it will be appreciated that the method of the present invention may also include modulation of the PNS, or both the SNS and the PNS. Components of the PNS that can be modulated according to the present invention include, but are not limited to, descending components of the vagus nerve, preganglionic PNS fibers traveling with SNS fibers in the celiac plexus, the aorto-renal ganglion, and ascending PNS inputs into the kidney(s) (e.g., from the sacral plexus and the pelvic splanchnic nerves with inputs from the inferior hypogastric plexus, the superior hypogastric plexus, and the intermesenteric plexus).

In another embodiment of the present invention, the method 200 can include implanting an expandable support member 12a and a branch member 22 at first and second desired vascular locations, respectively, so that at least a portion of each of the expandable support member and the branch member are positioned substantially adjacent the first and second desired vascular locations. As shown in Fig. 20, the first desired vascular location includes the abdominal aorta 58 proximate the renal arteries 54 and 56, and the second desired vascular location includes the left renal artery. The expandable support member 12a may be identically constructed as the expandable support member in Fig. 13, and the branch member 22 may be identically constructed as the branch members in Fig. 2, except where as described below.

As shown in Fig. 20, at least one magnetic member 110 may be securely attached to each of the expandable support member 12a and the branch member 22. The magnetic member 110 may be made of any one or combination of known electromagnetic materials including, for example, iron, NdFeB, SmCO and Alnico.
The magnetic member 110 may be securely attached to each of the expandable support member 12 and the branch member 22 using any suitable means known in the art including, for example, soldering, staples, clips, sutures, and/or adhesives. The magnetic member 110 may be attached to each of the expandable support member 12 and the branch member 22 at any desired vascular location, such as at the first and second end portions 24 and 26 of the expandable support member and the first and second end portions 23 and 25 of the branch member. The magnetic member 110 may have any suitable shape or configuration including, for example, a circular shape, an ovoid shape, a square-like shape, and/or a rectangular shape.

Alternatively or additionally, the magnetic member 110 may have a ring-like shape to completely encircle the expandable support member 12 and/or the branch member 22.

The expandable support member 12 and the branch member 22 may be implanted at the first and second desired vascular locations, respectively, using a minimally invasive, percutaneous, or endovascular approach as described above. The expandable support member 12 and the branch member 22 may be respectively implanted in an arterial and venous vessel, in first and second arterial vessels, and/or in first and second venous vessels. As shown in Fig. 20, for example, the expandable support member 12 and the branch member 22 may be respectively implanted in an abdominal aorta 58 proximate the renal arteries 54 and 56 and a left renal artery 54 using a percutaneous approach (as described above).

After the expandable support member 12 and the branch member 22 are securely positioned at the first and second desired vascular locations, an electromagnetic force may be generated between the magnetic members 110 connected to each of the expandable support member and the branch member. As indicated by the directional lines in Fig. 20, the magnetic members 110 are polarized upon placement and consequently generate an electric current between one another. The electric current may be distributed across the electrodes 16 of the expandable support member 12 and the branch member 22 and then delivered to the first and second desired vascular locations. By adjusting the size, number, and composition of the magnetic members 110, in addition to the position of the
expandable support member 12a and the branch member 22, the magnitude and
direction of the electric current may be varied as needed.

In another embodiment of the present invention, the method 200 can
include implanting an expandable support member 12a at a desired location
comprising a portion of the left renal artery 54 and the abdominal aorta 58. More
particularly, the expandable support member 12a can be implanted at a distal end
portion of the left renal artery 54. When the expandable support member 12a is
implanted at the desired location, the first end portion 24a can expand into a
portion of the abdominal aorta 58 and the second end portion 26a can expand into a
proximal end portion of the left renal artery 54 so that the electrodes 16 at the first
and second end portions are adjacent the left aorticorenal ganglion 76 and the renal
nerves 72, respectively. Electric current can then be delivered to the electrodes 16
(as described above) to selectively modulate the SNS, the PNS, or both and thereby
affect renal function.

It should be appreciated that the present invention can also include an
extravascular approach to renal neuromodulation. Using laparoscopic surgery, for
example, a neuromodulation device 10a similar or identical to the neuromodulation
device of Fig. 12 may be placed in a cuff-like manner around a desired
extravascular location, such as the proximal portion of the left renal artery 54
(Fig. 21). Electrical energy may then be delivered to the electrodes 16 of the
neuromodulation device 10a, thereby modulating effentner nerve fibers emanating
from the left aorticorenal ganglion 76 and thus altering renal function. It will be
appreciated that the apparatus 10a may be placed at other desired locations to
directly modulation renal function. For example, the apparatus 10a may be placed
at or near the cervical-thoracic segments of the sympathetic ganglia, including both
pre- and post-ganglionic ganglia. Additionally or alternatively, the apparatus 10a
may be placed at or near the renal capsule, the adipose capsule, or the renal fascia
to directly modulate renal function.

From the above description of the invention, those skilled in the art will
perceive improvements, changes and modifications. Such improvements, changes,
and modifications are within the skill of the art and are intended to be covered by
the appended claims.
Having described the invention, we claim:

1. A method for treating a renal disease or disorder, said method comprising the steps of:
   determining the geometry of a desired vascular location where modulation of the sympathetic nervous system (SNS) is possible;
   adjusting the geometry of an implantable neuromodulation device to correspond to the geometry of the desired vascular location;
   implanting the neuromodulation device at the desired vascular location; and
   delivering electric current to the neuromodulation device to effect a change in the SNS.

2. The method of claim 1, wherein said step of adjusting the geometry of an implantable neuromodulation device further comprises providing an implantable neuromodulation device comprising an expandable support member having a main body portion for engaging a wall of a blood vessel proximate a renal vasculature, at least one electrode connected with the main body portion arranged to selectively deliver electric current to a desired location, and an insulative material attached to at least a portion of the main body portion for isolating blood flow through the vessel from the electric current delivered by the at least one electrode.

3. The method of claim 2 further including shaping a portion of the expandable support member to correspond to the geometry of a blood vessel lumen.

4. The method of claim 1, wherein said step of determining the geometry of a desired vascular location further includes using an imaging modality to determine at least one characteristic of the desired vascular location selected from the group consisting of blood vessel length, blood vessel circumference, blood vessel perimeter, blood vessel area, blood flow, and transmural pressure.
5. The method of claim 1, wherein said step of implanting the neuromodulation device includes positioning a portion of the neuromodulation device substantially adjacent a desired vascular location where modulation of the parasympathetic nervous system (PNS) and the SNS is effective to alter renal function.

6. The method of claim 1, wherein said step of implanting the neuromodulation device includes positioning at least a portion of the neuromodulation device substantially adjacent a desired vascular location where modulation of the PNS is effective to alter renal function.

7. The method of claim 1, wherein the change in the SNS includes a change in neurohormonal activation.

8. The method of claim 1, wherein said step of implanting the neuromodulation device further includes positioning at least a portion of the neuromodulation device substantially adjacent a desired vascular location in an aortic arterial wall.

9. The method of claim 1, wherein said step of implanting the neuromodulation device further includes positioning at least a portion of the neuromodulation device substantially adjacent a desired vascular location in a vena cava venous wall.

10. The method of claim 1, wherein the change in the SNS is chemically induced by at least one pharmacological agent associated with the neuromodulation device.

11. The method of claim 1, wherein the change in the SNS is biologically induced by at least one biological agent associated with the neuromodulation device.
12. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates the level of renin.

13. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates at least one of urine production and blood pressure.

14. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates vasoconstriction or blood vessel tone.

15. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates efferent neuronal activity.

16. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates afferent neuronal activity.

17. The method of claim 1, wherein delivery of electric current to the neuromodulation device modulates both efferent and afferent neuronal activity.

18. A method for treating a renal disease or disorder, said method comprising the steps of:
   determining the geometry of a desired vascular location where modulation of the sympathetic nervous system (SNS) is possible;
   providing an implantable neuromodulation device comprising an expandable support member having a main body portion for engaging a wall of a blood vessel proximate a renal vasculature, at least one electrode connected with the main body portion arranged to selectively deliver electric current to a desired location, and an insulative material attached to at least a portion of the main body portion for isolating blood flow through the vessel from the electric current delivered by the at least one electrode;
   adjusting the geometry of the implantable neuromodulation device to correspond to the geometry of the desired vascular location;
implanting the neuromodulation device at the desired vascular location; and
delivering electric current to the neuromodulation device to effect a change in the SNS.

19. The method of claim 18 further including shaping a portion of the expandable support member to correspond to the geometry of a blood vessel lumen.

20. The method of claim 18, wherein said step of determining the geometry of a desired vascular location further includes using an imaging modality to determine at least one characteristic of the desired vascular location selected from the group consisting of blood vessel length, blood vessel circumference, blood vessel perimeter, blood vessel area, blood flow, and transmural pressure.

21. The method of claim 18, wherein said step of implanting the main body portion includes positioning the at least one electrode substantially adjacent a desired vascular location where modulation of the parasympathetic nervous system (PNS) and the SNS is effective to alter renal function.

22. The method of claim 18, wherein said step of implanting the main body portion includes positioning the at least one electrode substantially adjacent a desired vascular location where modulation of the PNS is effective to alter renal function.

23. The method of claim 18, wherein the change in the SNS includes a change in neurohormonal activation.

24. The method of claim 18, wherein said step of implanting the main body portion further includes positioning at least a portion of the main body portion substantially adjacent a desired vascular location in an aortic arterial wall.
25. The method of claim 18, wherein said step of implanting the main body portion further includes positioning at least a portion of the main body portion substantially adjacent a desired vascular location in a vena cava venous wall.

26. The method of claim 18, wherein the change in the SNS is chemically induced by at least one pharmacological agent associated with the expandable support member.

27. The method of claim 18, wherein the change in the SNS is biologically induced by at least one biological agent associated with the expandable support member.

28. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates the level of renin.

29. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates at least one of urine production and blood pressure.

30. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates vasoconstriction or blood vessel tone.

31. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates efferent neuronal activity.

32. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates afferent neuronal activity.

33. The method of claim 18, wherein delivery of electric current to the at least one electrode modulates both efferent and afferent neuronal activity.
Fig. 1

DETERMINING THE GEOMETRY OF A DESIRED VASCULAR LOCATION

ADJUSTING THE GEOMETRY OF AN IMPLANTABLE NEUROMODULATION DEVICE

IMPLANTING THE NEUROMODULATION DEVICE AT THE DESIRED VASCULAR LOCATION

DELIVERING ELECTRIC CURRENT TO THE NEUROMODULATION DEVICE
Applicant's or agent's file reference  
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Applicant  
THE CLEVELAND CLINIC FOUNDATION

This International Searching Authority hereby declares, according to Article 17(2)(a), that no international search report will be established on the international application for the reasons indicated below:

1. [X] The subject matter of the international application relates to:
   a. [] scientific theories
   b. [] mathematical theories
   c. [] plant varieties
   d. [] animal varieties
   e. [] essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes
   f. [] schemes, rules or methods of doing business
   g. [] schemes, rules or methods of performing purely mental acts
   h. [] schemes, rules or methods of playing games
   i. [X] methods for treatment of the human body by surgery or therapy
   j. [X] methods for treatment of the animal body by surgery or therapy
   k. [] diagnostic methods practised on the human or animal body
   l. [] mere presentations of information
   m. [] computer programs for which this International Searching Authority is not equipped to search prior art

2. [] The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:
   a. [] the description
   b. [] the claims
   c. [] the drawings

3. [] A meaningful search could not be carried out without the sequence listing; the applicant did not, within the prescribed time limit:
   a. [] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
   b. [] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
   c. [] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

4. [] A meaningful search could not be carried out without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

5. Further comments:

Name and mailing address of the International Searching Authority  
European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Fax. (+31-70) 311-651 epo nl

Authorized officer  
Hans Van Brummelen

Form PCT/ISA/203 (April 2005)
A meaningful search is not possible on the basis of all claims because all claims are directed to - Method for treatment of the human or animal body by surgery and therapy - Rule 39.1(iv) PCT

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 Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.