

(12) STANDARD PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. **AU 2010229985 B2**

(54) Title
Pain management with stimulation subthreshold to paresthesia

(51) International Patent Classification(s)
A61N 1/36 (2006.01) **A61N 1/05** (2006.01)

(21) Application No: **2010229985** (22) Date of Filing: **2010.03.24**

(87) WIPO No: **WO10/111358**

(30) Priority Data

(31) Number	(32) Date	(33) Country
61/163,007	2009.03.24	US

(43) Publication Date: **2010.09.30**

(44) Accepted Journal Date: **2015.09.17**

(71) Applicant(s)
Spinal Modulation, Inc.

(72) Inventor(s)
Kishawi, Eyad;Kramer, Jeffery M.

(74) Agent / Attorney
Pizzeys Patent and Trade Mark Attorneys, GPO Box 1374, BRISBANE, QLD, 4001

(56) Related Art
US 6002964
US 2008/0140169
US 2006/0052839

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 September 2010 (30.09.2010)

(10) International Publication Number
WO 2010/111358 A3

(51) International Patent Classification:

A61N 1/36 (2006.01) A61N 1/05 (2006.01)

(21) International Application Number:

PCT/US2010/028450

(22) International Filing Date:

24 March 2010 (24.03.2010)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/163,007 24 March 2009 (24.03.2009) US

(71) Applicant (for all designated States except US): **SPINAL MODULATION, INC.** [US/US]; 1135 O'Brien Drive, Menlo Park, CA 94025 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KISHAWI, Eyad** [US/US]; 1135 O'Brien Drive, Menlo Park, CA 94025 (US). **KRAMER, Jeffery, M.** [US/US]; 1135 O'Brien Drive, Menlo Park, CA 94025 (US).

(74) Agents: **GLENN, Benjamin, W.** et al.; Shay Glenn LLP, 2755 Campus Drive, Suite 210, San Mateo, CA 94403 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

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

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

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

13 January 2011

(54) Title: PAIN MANAGEMENT WITH STIMULATION SUBTHRESHOLD TO PARASTHESIA

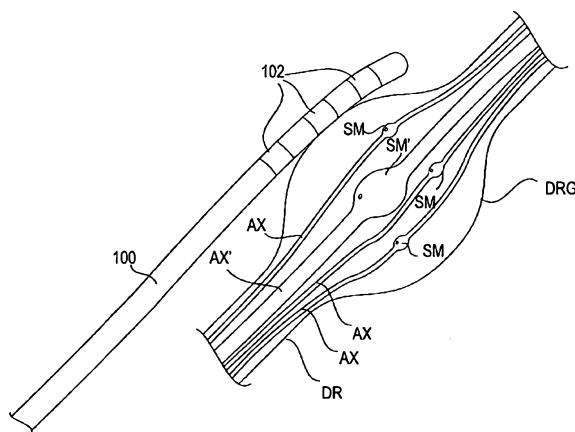


FIG. 4

(57) Abstract: Devices, systems and methods are provided for treating pain while minimizing or eliminating possible complications and undesired side effects, particularly the sensation of paresthesia. This is achieved by stimulating in proximity to a dorsal root ganglion with stimulation energy in a manner that will affect pain sensations without generating substantial sensations of paresthesia. In some embodiments, such neurostimulation takes advantage of anatomical features and functions particular to the dorsal root ganglion.

WO 2010/111358 A3

PAIN MANAGEMENT WITH STIMULATION SUBTHRESHOLD TO PARASTHESIA

CROSS-REFERENCES TO RELATED APPLICATIONS

5 [0001] This application claims priority under 35 U.S.C. 119(e) to U.S. Provisional Patent Application No. 61/163,007, entitled "Pain Management with Subthreshold Stimulation", filed March 24, 2009, which is incorporated herein by reference.

STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

10 [0002] NOT APPLICABLE

REFERENCE TO A "SEQUENCE LISTING," A TABLE, OR A COMPUTER PROGRAM LISTING APPENDIX SUBMITTED ON A COMPACT DISK.

[0003] NOT APPLICABLE

15

BACKGROUND OF THE INVENTION

[0004] For more than 30 years, spinal cord stimulation (SCS) has been used to treat a variety of pain syndromes. The goal of SCS is to create paresthesia that completely and consistently covers the painful areas, yet does not cause uncomfortable sensations in other areas. Paresthesia may be defined as a sensation of tingling, pricking, or numbness in an area of the body. It is more generally known as the feeling of "pins and needles". In some instances, the feeling of paresthesia is preferred over the feeling of pain. In SCS, paresthesia production is accomplished by stimulating A β fibers in the dorsal column and/or the dorsal roots. Dorsal column stimulation typically causes paresthesia in several dermatomes at and below the level of the stimulator. In contrast, dorsal root stimulation activates fibers in a limited number of rootlets in close proximity to the stimulator and causes paresthesia in only a few dermatomes. Because of these factors, dorsal root stimulation with an SCS stimulator may not produce sufficient pain relief. In addition, stimulation of the roots with an SCS stimulator can cause uncomfortable sensations and motor responses. These side effects may occur at pulse amplitudes that are below the value needed for full paresthesia coverage. Therefore, the clinical goal of SCS is to produce an electrical field that stimulates the relevant spinal cord structures without stimulating the nearby nerve root.

20
25
30

[0005] Intraspinal nerve root stimulation is a technique related to SCS, except that electrodes are placed along the nerve rootlets in the lateral aspect of the spinal canal (this area is known as “the gutter”), rather than over the midline of the spinal cord. The electrodes are mounted on a cylindrical lead rather than on a traditional SCS paddle lead. The accuracy of the leads'

5 placement within the gutter is confirmed by stimulating the nerve roots at perceptible levels, which result in paresthesia in the local area. Sensory paresthesia may be generated by stimulating at a level above the threshold for sensory recruitment. This may be used in conjunction with SCS to treat certain pain conditions.

[0006] For some patients, paresthesia is an undesired effect and is not a well tolerated
10 alternative to pain. Therefore, improved treatments are needed to provide pain relief with minimal undesired effects. At least some of these objectives will be met by the present invention.

BRIEF SUMMARY OF THE INVENTION

[0007] The present invention provides devices, systems and methods for treating conditions, such as pain, while minimizing or eliminating possible complications and undesired side effects.

15 In particular, the devices, systems and methods treat pain without generating substantial sensations of paresthesia. This is achieved by stimulating in proximity to a dorsal root ganglion with specific stimulation energy levels, as will be described in more detail herein.

[0008] In a first aspect of the present invention, a method is provided of treating pain in a patient comprising positioning a lead having at least one electrode disposed thereon so that at
20 least one of the at least one electrode is in proximity to a dorsal root ganglion, and providing stimulation energy to the at least one of the at least one electrode so as to stimulate at least a portion of the dorsal root ganglion. Together the positioning of the lead step and the providing stimulation energy step affect pain sensations without generating substantial sensations of paresthesia.

25 [0009] In some embodiments, providing stimulation energy comprises providing stimulation energy at a level below a threshold for A β fiber recruitment. And, in some embodiments, providing stimulation energy comprises providing stimulation energy at a level below a threshold for A β fiber cell body recruitment.

[0010] In other embodiments, providing stimulation energy comprises: a) providing
30 stimulation energy at a level above a threshold for A δ fiber cell body recruitment, b) providing stimulation energy at a level above a threshold for C fiber cell body recruitment, c) providing stimulation energy at a level above a threshold for small myelinated fiber cell body recruitment,

or d) providing stimulation energy at a level above a threshold for unmyelinated fiber cell body recruitment.

[0011] In still other embodiments, providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating glial cell function within the dorsal root ganglion. For example, in some embodiments, providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating satellite cell function within the dorsal root ganglion. In other embodiments, providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating Schwann cell function within the dorsal root ganglion.

[0012] In yet other embodiments, providing stimulation energy comprises providing stimulation energy at a level which is capable of causing at least one blood vessel associated with the dorsal root ganglion to release an agent or send a cell signal which affects a neuron or glial cell within the dorsal root ganglion.

[0013] In some embodiments, positioning the lead comprises advancing the lead through an epidural space so that at least a portion of the lead extends along a nerve root sleeve angulation. And, in some instances advancing the lead through the epidural space comprises advancing the lead in an antegrade direction.

[0014] In a second aspect of the present invention, a method is provided for treating a patient comprising selectively stimulating a small fiber cell body within a dorsal root ganglion of the patient while excluding an A β fiber cell body with the dorsal root ganglion of the patient. In some embodiments, the small fiber body comprises an A δ fiber cell body. In other embodiments, the small fiber body comprises a C fiber cell body.

[0015] In a third aspect of the present invention, a method is provided for treating a patient comprising identifying a dorsal root ganglion associated with a sensation of pain by the patient, and neuromodulating at least one glial cell within the dorsal root ganglion so as to reduce the sensation of pain by the patient. In some embodiments, the at least one glial cell comprises a satellite cell. In other embodiments, the at least one glial cell comprises a Schwann cell. And, in some embodiments, neuromodulating comprises providing stimulation at a level that reduces the sensation of pain without generating substantial sensations of paresthesia.

[0016] In a fourth aspect of the present invention, a method is provided for treating a patient comprising positioning a lead having at least one electrode disposed thereon so that at least one of the at least one electrode is in proximity to a dorsal root ganglion, and providing stimulation energy to the at least one electrode so as to stimulate at least one blood vessel associated with the

dorsal root ganglion in a manner that causes the at least one blood vessel to release an agent which neuromodulates a neuron within the dorsal root ganglion. In some embodiments, the agent comprises a neuromodulatory chemical that affects the function of neurons involved in pain sensory transduction.

5 [0017] In a fifth aspect of the present invention, a system is provided for treating pain in a patient comprising a lead having at least one electrode disposed thereon, wherein the lead is configured for placement in proximity to a dorsal root ganglion, and a pulse generator configured to provide stimulation energy to the at least one of the at least one electrode while the lead is positioned in proximity to the dorsal root ganglion so as to stimulate at least a portion of the
10 dorsal root ganglion in a manner which affects pain sensations without generating substantial sensations of paresthesia.

[0018] In some embodiments, the pulse generator provides stimulation energy at a level at below a threshold for A β fiber recruitment. In other embodiments, the pulse generator provides stimulation energy at a level below a threshold for A β fiber cell body recruitment. In other
15 embodiments, the pulse generator provides stimulation energy at a level above a threshold for A δ fiber cell body recruitment. In still other embodiments, the pulse generator provides stimulation energy at a level above a threshold for C fiber cell body recruitment. In some embodiments, the pulse generator provides stimulation energy at a level above a threshold for small myelinated fiber cell body recruitment. And, in some embodiments, the pulse generator provides
20 stimulation energy at a level above a threshold for unmyelinated fiber cell body recruitment.

[0019] In some embodiments, the pulse generator provides stimulation energy at a level which is capable of modulating glial cell function within the dorsal root ganglion. For example, in some embodiments, the pulse generator provides stimulation energy at a level which is capable of modulating satellite cell function within the dorsal root ganglion. In other embodiments, the
25 pulse generator provides stimulation energy at a level which is capable of modulating Schwann cell function within the dorsal root ganglion.

[0020] In some instances, the pulse generator provides stimulation energy at a level which is capable of causing at least one blood vessel associated with the dorsal root ganglion to release an agent or send a cell signal which affects a neuron or glial cell within the dorsal root ganglion.

30 [0021] And, in some embodiments, the lead is configured to be advanced in an antegrade direction through an epidural space and positioned so that at least a portion of the lead extends along a nerve root sleeve angulation.

[0022] Other objects and advantages of the present invention will become apparent from the detailed description to follow, together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] Fig. 1A provides a schematic illustration of a spinal cord, associated nerve roots and a peripheral nerve on a spinal level and Fig. 1B illustrates cells within a DRG.

[0024] Figs. 2A-2C provide a cross-sectional histological illustration of a spinal cord and a DRG under varying levels of magnification.

[0025] Fig. 3 illustrates an embodiment of a lead, having at least one electrode thereon, advanced through the patient anatomy so that at least one of the electrodes is positioned on a target DRG.

[0026] Fig. 4 provides a schematic illustration of the lead positioned on a DRG.

[0027] Fig. 5 illustrates a graph showing an example relationship between threshold stimulus and nerve fiber diameter.

[0028] Fig. 6 illustrates recruitment order based on nerve fiber diameter.

[0029] Fig. 7 illustrates recruitment order based on cell body size.

[0030] Fig. 8 illustrates recruitment order differences based on location of stimulation.

[0031] Fig. 9 provides a schematic illustration of an embodiment of the lead positioned on a DRG, including various cells and anatomical structures associated with the DRG.

[0032] Figs. 10A-10D, 11, 12 illustrate embodiments of a lead and delivery system.

DETAILED DESCRIPTION OF THE INVENTION

[0033] The present invention provides devices, systems and methods for treating pain while minimizing or eliminating possible complications and undesired side effects, particularly the sensation of paresthesia. This is achieved by stimulating in proximity to a dorsal root ganglion with stimulation energy in a manner that will affect pain sensations without generating substantial sensations of paresthesia. In some embodiments, such neurostimulation takes advantage of anatomical features and functions particular to the dorsal root ganglion, as will be described in more detail below. The devices, systems and methods are minimally invasive, therefore reducing possible complications resulting from the implantation procedure, and targeted so as to manage pain sensations with minimal or no perceptions such as paresthesia.

[0034] Fig. 1A provides a schematic illustration of a spinal cord S, associated nerve roots and a peripheral nerve on a spinal level. Here, the nerve roots include a dorsal root DR and a ventral root VR that join together at the peripheral nerve PN. The dorsal root DR includes a dorsal root ganglion DRG, as shown. The DRG is comprised of a variety of cells, including large neurons, small neurons and non-neuronal cells. Each neuron in the DRG is comprised of a bipolar or quasi-unipolar cell having a soma (the bulbous end of the neuron which contains the cell nucleus) and two axons. The word soma is Greek, meaning "body"; the soma of a neuron is often called the "cell body". Somas are gathered within the DRG, rather than the dorsal root, and the associated axons extend therefrom into the dorsal root and toward the peripheral nervous system. Fig. 1B provides an expanded illustration of cells located in the DRG, including a small soma SM, a large soma SM' and non-neuronal cells (in this instance, satellite cells SC). Figs. 2A-2C provide a cross-sectional histological illustration of a spinal cord S and associated nerve roots, including a DRG. Fig. 2A illustrates the anatomy under 40X magnification and indicates the size relationship of the DRG to the surrounding anatomy. Fig. 2B illustrates the anatomy of Fig. 2A under 100X magnification. Here, the differing structure of the DRG is becoming visible. Fig. 2C illustrates the anatomy of Fig. 2A under 400X magnification focusing on the DRG. As shown, the larger soma SM' and the smaller somas SM are located within the DRG.

[0035] In some embodiments, stimulation of a DRG according to the present invention is achieved with the use of a lead having at least one electrode thereon. The lead is advanced through the patient anatomy so that the at least one electrode is positioned on, near, about or in proximity to the target DRG. The lead and electrode(s) are sized and configured so that the electrode(s) are able to minimize or exclude undesired stimulation of other anatomies.

[0036] Fig. 3 illustrates an embodiment of a lead 100, having at least one electrode 102 thereon, advanced through the patient anatomy so that at least one of the electrodes 102 is positioned on a target DRG. In this example, the lead 100 is inserted epidurally and advanced in an antegrade direction along the spinal cord S. As shown, each DRG is disposed along a dorsal root DR and typically resides at least partially between the pedicles PD or within a foramen. Each dorsal root DR exits the spinal cord S at an angle θ . This angle θ is considered the nerve root sleeve angulation and varies slightly by patient and by location along the spinal column. However, the average nerve root angulation is significantly less than 90 degrees and typically less than 45 degrees. Therefore, advancement of the lead 100 toward the target DRG in this manner involves making a sharp turn along the angle θ . A turn of this severity is achieved with the use of delivery tools and design features specific to such lead placement which will be described in more detail in later sections. In addition, the spatial relationship between the nerve

roots, DRGs and surrounding structures are significantly influenced by degenerative changes, particularly in the lumbar spine. Thus, patients may have nerve root angulations which differ from the normal anatomy, such as having even smaller angulations necessitating even tighter turns. The delivery tools and devices accommodate these anatomies.

5 [0037] Fig.4 provides a schematic illustration of an embodiment of the lead 100 positioned on a DRG. As illustrated, the DRG includes smaller somas SM and larger somas SM'. Each soma is connected with an associated axon or nerve fiber which extends through the root. The axon or nerve fiber is a long, slender projection of a nerve cell, or neuron that conducts electrical impulses away from the neuron's cell body or soma. The smaller somas SM have smaller axons
10 AX and the larger somas SM' have larger axons AX'. Typically, axons or nerve fibers are recruited electrically according to size. Referring to Fig. 5, a graph is provided which illustrates an example relationship between threshold stimulus and nerve fiber diameter. Generally, as the nerve fiber diameter increases, the threshold stimulus decreases. Thus, as illustrated in Fig. 6, larger myelinated fibers (A β fibers) are recruited before smaller myelinated fibers (A δ fibers),
15 which are in turn recruited before small unmyelinated fibers (C fibers).

[0038] Referring to Fig. 7, the opposite is true of cell bodies compared to nerve fibers. Generally, it takes less current to recruit or modulate a smaller cell body or soma membrane than a larger one. Thus, as shown in Fig. 8, when low stimulation is provided in region A (to the cell
20 bodies SM', SM) the smaller diameter cell bodies SM are selectively stimulated before the larger diameter cell bodies SM'. This is due to the relatively smaller charge it takes to effectively modulate membrane function of a smaller cell body. However, when low stimulation is provided in region B (to the axons AX' , AX) the larger axons AX' are stimulated before the smaller axons AX. Referring back to Fig. 4, since the cell bodies or somas are located within the DRG, region A generally corresponds to the DRG and region B generally corresponds to the dorsal root DR.

25 [0039] When a patient experiences pain, the nociceptive or painful stimuli are transduced from peripheral structures to the central nervous systems through small diameter, thinly myelinated and unmyelinated afferent nerve fibers or axons AX. Electrically, these fibers are more difficult to selectively target since larger diameter fibers or axons AX' are preferentially activated by electrical currents based upon the above described size principle. These larger fibers AX' are
30 associated with sensory stimuli such as light touch, pressure and vibration and well as paresthesia such as generated by SCS.

[0040] The present invention provides methods and devices for preferentially neuromodulating the smaller diameter axon/smaller soma neurons over the larger diameter axon/larger soma

neurons. This in turn interrupts pain transmission while minimizing or eliminating paresthesia. Referring again to Fig. 4, an example is illustrated of a lead 100 positioned so that at least one of the electrodes 102 is disposed so as to selectively stimulate the DRG while minimizing or excluding undesired stimulation of other anatomies, such as portions of the dorsal root DR. This allows the smaller diameter axon/smaller soma neurons to be recruited before the larger diameter axon/larger soma neurons. Consequently, these neurons involved in pain transduction can be modulated without producing paresthesias. This is achieved with the use of less current or lower power stimulation, i.e. stimulation at a subthreshold level to paresthesia. The effect of this preferential, targeted neuromodulation is analgesia without resultant paresthesias. In addition, lower power stimulation means lower power consumption and longer battery life.

[0041] Conventional spinal stimulation systems typically provide stimulation with a frequency of about 30 - 120 Hz. In contrast, therapeutic benefits have been achieved with the devices and methods described herein at stimulation frequencies below those used in conventional stimulation systems. In one aspect, the stimulation frequency used for the DRG stimulation methods described herein is less than 25 Hz. In other aspects, the stimulation frequency could be even lower such as in the range of less than 15 Hz. In still other aspects, the stimulation frequency is below 10Hz. In one specific embodiment, the stimulation frequency is 5 Hz. In another specific, embodiment, the stimulation frequency is 2 Hz. In addition to lower stimulation frequencies, other stimulation patterns for the inventive devices and methods are also lower than those used in conventional stimulation systems. For example, embodiments of the present invention have achieved repeatable dermatome specific pain relief using a stimulation signal having an amplitude of less than 500 microamps, a pulse width of less than 120 microseconds and a low stimulation frequency as discussed above. It is believed that embodiments of the present invention can achieve dermatome specific pain relief using signals having pulse widths selected within the range of 60 microseconds to 120 microseconds. It is believed that embodiments of the present invention can achieve dermatome specific pain relief using a signal having an amplitude of about 200 microamps. In one specific example, repeatable dermatome specific pain relief was achieved in an adult female using a signal with an amplitude of 200 microamps, a pulse width of 60 microseconds and a frequency of 2 Hz. It may also be appreciated that other suitable stimulation signal parameters may be used along, such as provided in US Patent Application No. 12/607,009 entitled "Selective Stimulation Systems and Signal Parameters For Medical Conditions", filed October 27, 2009, incorporated herein by reference for all purposes.

[0042] In addition to neuronal cells, non-neuronal cells, such as glial cells, are located within the DRG. Glial cells surround neurons, hold them in place, provide nutrients, help maintain homeostasis, provide electrical insulation, destroy pathogens, regulate neuronal repair and the removal dead neurons, and participate in signal transmission in the nervous system. In addition, glial cells help in guiding the construction of the nervous system and control the chemical and ionic environment of the neurons. Glial cells also play a role in the development and maintenance of dysfunction in chronic pain conditions. A variety of specific types of glial cells are found within the DRG, such as satellite cells and Schwann cells.

[0043] Satellite cells surround neuron cell bodies within the DRG. They supply nutrients to the surrounding neurons and also have some structural function. Satellite cells also act as protective, cushioning cells. In addition, satellite cells can form gap junctions with neurons in the DRG. As opposed to classical chemical transmission in the nervous system, gap junctions between cells provide a direct electrical coupling. This, in turn, can produce a form of a quasi glial-neuronal syncytium. Pathophysiologic conditions can change the relationship between glia and cell bodies such that the neurons transducing information about pain can become dysfunctional. Therefore neurostimulation of the DRG can not only directly affect neurons but also impact the function of glial cells. Modulation of glial cell function with neurostimulation can in turn alter neuronal functioning. Such modulation can occur at levels below a threshold for generating sensations of paresthesia.

[0044] Fig.9 provides a schematic illustration of an embodiment of the lead 100 positioned on a DRG. As illustrated, the DRG includes satellite cells SC surrounding smaller somas SM and larger somas SM'. In some embodiments, stimulation energy provided by at least one of the electrodes 102 neuromodulates satellite cells SC. Such neuromodulation impacts their function and, secondarily, impacts the function of associated neurons so as to interrupt or alter processing of sensory information, such as pain. Consequently, DRG satellite cell neuromodulation can be a treatment for chronic pain.

[0045] Another type of glial cells are Schwann cells. Also referred to as neurolemnocytes, Schwann cells assist in neuronal survival. In myelinated axons, Schwann cells form the myelin sheath. The vertebrate nervous system relies on the myelin sheath for insulation and as a method of decreasing membrane capacitance in the axon. The arrangement of the Schwann cells allows for saltatory conduction which greatly increases speed of conduction and saves energy. Non-myelinating Schwann cells are involved in maintenance of axons. Schwann cells also provide axon support, trophic actions and other support activities to neurons within the DRG.

[0046] Referring again to Fig.9, Schwann cells SWC are illustrated along the axons of a neuron within the DRG. In some embodiments, stimulation energy provided by at least one of the electrodes 102 of the lead 100 neuromodulates Schwann cells SWC. Such neuromodulation impacts their function and, secondarily, impacts the function of associated neurons.

5 Neuromodulation of Schwann cells impacts neuronal processing, transduction and transfer of sensory information including pain. Thus, DRG stimulation relieves pain in the short and long term by impacting function of Schwann cells. This also may be achieved at stimulation levels below a threshold for generating sensations of paresthesia.

[0047] Beyond the neural cells (neurons, glia, etc) that are present in the DRG, there is a rich
10 network of blood vessels that travel in and about the DRG to encapsulate the DRG and provide a blood supply and oxygen to this highly metabolically active neural structure. Fig. 9 schematically illustrates a blood vessel BV associated with and an example DRG. In some embodiments, stimulation energy is provided by at least one of the electrodes 102 of the lead 100. Stimulation of the DRG can cause the release of a variety of agents from the neurons, glia
15 and/or blood vessels which ultimately impact the function of neurons involved in the transduction and processing of sensory information, including pain. For example, in some embodiments stimulation of the DRG causes one or more types of neurons and/or one or more types of glial cells to release vasoactive agents which affect at least one blood vessel. The at least one blood vessel in turn releases neuronal agents impact the function of neurons in
20 processing pain. Or, the at least one blood vessel releases glial active agents which indirectly impacts the function of neurons in processing pain. In other embodiments, stimulation of the DRG directly affects the associated blood vessels which provide vessel to neuron cell signaling or vessel to glial cell signaling. Such cell signaling ultimately impacts neuronal function, such as by altering metabolic rate or inducing the release of neural responsive chemicals which, in turn,
25 directly change the cell function. The change in cell function induces analgesia or pain relief in the short-term, mid-term and long-term. Such changes may occur at stimulation levels below a threshold for generating sensations of paresthesia.

[0048] Desired positioning of a lead 100 near the target anatomy, such as the DRG, may be achieved with a variety of delivery systems, devices and methods. Referring back to Fig. 3, an
30 example of such positioning is illustrated. In this example, the lead 100 is inserted epidurally and advanced in an antegrade direction along the spinal cord S. As shown, each DRG is disposed along a dorsal root DR and typically resides at least partially between the pedicles PD or within a foramen. Each dorsal root DR exits the spinal cord S at an angle θ . This angle θ is considered the nerve root sleeve angulation and varies slightly by patient and by location along

the spinal column. However, the average nerve root angulation is significantly less than 90 degrees and typically less than 45 degrees. Therefore, advancement of the lead 100 toward the target DRG in this manner involves making a sharp turn along the angle θ . In addition, the spatial relationship between the nerve roots, DRGs and surrounding structures are significantly influenced by degenerative changes, particularly in the lumbar spine. Thus, patients may have nerve root angulations which differ from the normal anatomy, such as having even smaller angulations necessitating even tighter turns. Turns of this severity are achieved with the use of delivery tools having design features specific to such lead placement.

[0049] Referring to Figs. 10A-10D, an example lead and delivery devices for accessing a target DRG are illustrated. Fig. 10A illustrates an embodiment of a lead 100 comprising a shaft 103 having a distal end 101 with four electrodes 102 disposed thereon. It may be appreciated that any number of electrodes 102 may be present, including one, two, three, four, five, six, seven, eight or more. In this embodiment, the distal end 101 has a closed-end distal tip 106. The distal tip 106 may have a variety of shapes including a rounded shape, such as a ball shape (shown) or tear drop shape, and a cone shape, to name a few. These shapes provide an atraumatic tip for the lead 100 as well as serving other purposes. The lead 100 also includes a stylet lumen 104 which extends toward the closed-end distal tip 106. A delivery system 120 is also illustrated, including a sheath 122 (Fig. 10B), stylet 124 (Fig. 10C) and introducing needle 126 (Fig. 10D).

[0050] Referring to Fig. 10B, an embodiment of a sheath 122 is illustrated. In this embodiment, the sheath 122 has a distal end 128 which is pre-curved to have an angle α , wherein the angle α is in the range of approximately 80 to 165 degrees. The sheath 122 is sized and configured to be advanced over the shaft 103 of the lead 100 until a portion of its distal end 128 abuts the distal tip 106 of the lead 100, as illustrated in Fig. 11. Thus, the ball shaped tip 106 of this embodiment also prevents the sheath 122 from extending thereover. Passage of the sheath 122 over the lead 100 causes the lead 100 to bend in accordance with the precurvature of the sheath 122. Thus, the sheath 122 assists in steering the lead 100 along the spinal column S and toward a target DRG, such as in a lateral direction.

[0051] Referring back to Fig. 10C, an embodiment of a stylet 124 is illustrated. The stylet 124 has a distal end 130 which is pre-curved so that its radius of curvature is in the range of approximately 0.1 to 0.5. The stylet 124 is sized and configured to be advanced within the stylet lumen 104 of the lead 100. Typically the stylet 124 extends therethrough so that its distal end 130 aligns with the distal end 101 of the lead 100. Passage of the stylet 124 through the lead 100 causes the lead 100 to bend in accordance with the precurvature of the stylet 124. Typically, the stylet 124 has a smaller radius of curvature, or a tighter bend, than the sheath 122. Therefore, as

shown in Fig. 12, when the stylet 124 is disposed within the lead 100, extension of the lead 100 and stylet 124 through the sheath 122 bends or directs the lead 100 through a first curvature 123. Further extension of the lead 100 and stylet 124 beyond the distal end 128 of the sheath 122 allows the lead 100 to bend further along a second curvature 125. This allows the laterally
5 directed lead 100 to now curve around toward the target DRG along the nerve root angulation. This two step curvature allows the lead 100 to be successfully positioned so that at least one of the electrodes 102 is on, near or about the target DRG, particularly by making a sharp turn along the angle θ .

[0052] Thus, the lead 100 does not require stiff or torqueable construction since the lead 100 is
10 not torqued or steered by itself. The lead 100 is positioned with the use of the sheath 122 and stylet 124 which direct the lead 100 through the two step curvature. This eliminates the need for the operator to torque the lead 100 and optionally the sheath 122 with multiple hands. This also allows the lead 100 to have a lower profile as well as a very soft and flexible construction. This, in turn, minimizes erosion and discomfort created by pressure on nerve tissue, such as the target
15 DRG and/or the nerve root, once the lead 100 is implanted. For example, such a soft and flexible lead 100 will minimize the amount of force translated to the lead 100 by body movement (e.g. flexion, extension, torsion).

[0053] Referring back to Fig. 10D, an embodiment of an introducing needle 126 is illustrated. The introducing needle 126 is used to access the epidural space of the spinal cord S. The needle
20 126 has a hollow shaft 127 and typically has a very slightly curved distal end 132. The shaft 127 is sized to allow passage of the lead 100, sheath 122 and stylet 124 therethrough. In some embodiments, the needle 126 is 14 gauge which is consistent with the size of epidural needles used to place conventional percutaneous leads within the epidural space. However, it may be appreciated that other sized needles may also be used, particularly smaller needles such as 16-18
25 gauge. Likewise, it may be appreciated that needles having various tips known to practitioners or custom tips designed for specific applications may also be used. The needle 126 also typically includes a Luer-LokTM fitting 134 or other fitting near its proximal end. The Luer-LokTM fitting 134 is a female fitting having a tabbed hub which engages threads in a sleeve on a male fitting, such as a syringe.

[0054] Methods of approaching a target DRG using such a delivery system 120 is further
30 described and illustrated in U.S. Patent Application No. 611144,690 filed January 14, 2009, incorporated herein by reference for all purposes, along with examples of other delivery systems, devices and methods applicable to use with the present invention.

[0055] It may be appreciated that other types of leads and corresponding delivery systems may be used to position such leads in desired orientations to provide stimulation subthreshold to parasthesia. For example, the lead may have a pre-curved shape wherein the lead is deliverable through a sheath having a straighter shape, such as a substantially straight shape or a curved shape which is has a larger radius of curvature than the lead. Advancement of the lead out of the sheath allows the lead to recoil toward its pre-curved shape. Various combinations of curvature between the lead and sheath may allow for a variety of primary and secondary curvatures. Once the lead is desirably placed, the sheath may then be removed.

[0056] It may also be appreciated that a variety of approaches to the DRG may be used, such as an antegrade epidural approach, a retrograde epidural approach, a transforaminal approach or an extraforaminal approach (approaching along a peripheral nerve from outside of the spinal column), and a contralateral approach, to name a few. Likewise, the at least one electrode may be positioned in, on or about, in proximity to, near or in the vicinity of the DRG.

[0057] Although the foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity of understanding, it will be obvious that various alternatives, modifications, and equivalents may be used and the above description should not be taken as limiting in scope of the invention which is defined by the appended claims.

CLAIMS

1. A method of treating pain in a patient comprising:
positioning a lead having at least one electrode disposed thereon so that at least one of the at least one electrode is in proximity to a dorsal root ganglion; and
providing stimulation energy to the at least one of the at least one electrode so as to stimulate at least a portion of the dorsal root ganglion,
wherein together the positioning of the lead step and the providing stimulation energy step reduce pain sensations without generating sensations of paresthesia.
2. A method as in claim 1, wherein providing stimulation energy comprises providing stimulation energy at a level below a threshold for A β fiber recruitment.
3. A method as in claim 2, wherein providing stimulation energy comprises providing stimulation energy at a level below a threshold for A β fiber cell body recruitment.
4. A method as in claim 3, wherein providing stimulation energy comprises providing stimulation energy at a level above a threshold for A δ fiber cell body modulation.
5. A method as in claim 3, wherein providing stimulation energy comprises providing stimulation energy at a level above a threshold for C fiber cell body modulation.
6. A method as in claim 3, wherein providing stimulation energy comprises providing stimulation energy at a level above a threshold for small myelinated fiber cell body modulation.

7. A method as in claim 3, wherein providing stimulation energy comprises providing stimulation energy at a level above a threshold for unmyelinated fiber cell body modulation.
8. A method as in claim 1, wherein providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating glial cell function within the dorsal root ganglion.
9. A method as in claim 8, wherein providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating satellite cell function within the dorsal root ganglion.
10. A method as in claim 8, wherein providing stimulation energy comprises providing stimulation energy at a level which is capable of modulating Schwann cell function within the dorsal root ganglion.
11. A method as in claim 1, wherein providing stimulation energy comprises providing stimulation energy at a level which is capable of causing at least one blood vessel associated with the dorsal root ganglion to release an agent or send a cell signal which affects a neuron or glial cell within the dorsal root ganglion.
12. A method as in claim 1, wherein positioning the lead comprises advancing the lead through an epidural space so that at least a portion of the lead extends along a nerve root sleeve angulation.
13. A method as in claim 12, wherein advancing the lead through the epidural space comprises advancing the lead in an antegrade direction.
14. A method of treating a patient comprising:

selectively electrically stimulating a small fiber cell body within a dorsal root ganglion of the patient while excluding an A β fiber cell body within the dorsal root ganglion of the patient.

15. A method as in claim 14, wherein the small fiber body comprises a A δ fiber cell body.
16. A method as in claim 14, wherein the small fiber body comprises a C fiber cell body.
17. A method of treating a patient comprising:
identifying a dorsal root ganglion associated with a sensation of pain by the patient; and
electrically neuromodulating at least one glial cell within the dorsal root ganglion so as to reduce the sensation of pain by the patient.
18. A method as in claim 17, wherein the at least one glial cell comprises a satellite cell.
19. A method as in claim 17, wherein the at least one glial cell comprises a Schwann cell.
20. A method as in claim 17, wherein neuromodulating comprises providing stimulation at a level that reduces the sensation of pain without generating substantial sensations of paresthesia.
21. A method of treating a patient comprising:
positioning a lead having at least one electrode disposed thereon so that at least one of the at least one electrode is in proximity to a dorsal root ganglion; and
providing stimulation energy to the at least one electrode so as to stimulate at least one blood vessel associated with the dorsal root ganglion in a manner that

causes the at least one blood vessel to release an agent which neuromodulates a neuron within the dorsal root ganglion.

22. A method as in claim 21, wherein the agent comprises a neuromodulatory chemical that affects the function of neurons involved in pain sensory transduction.

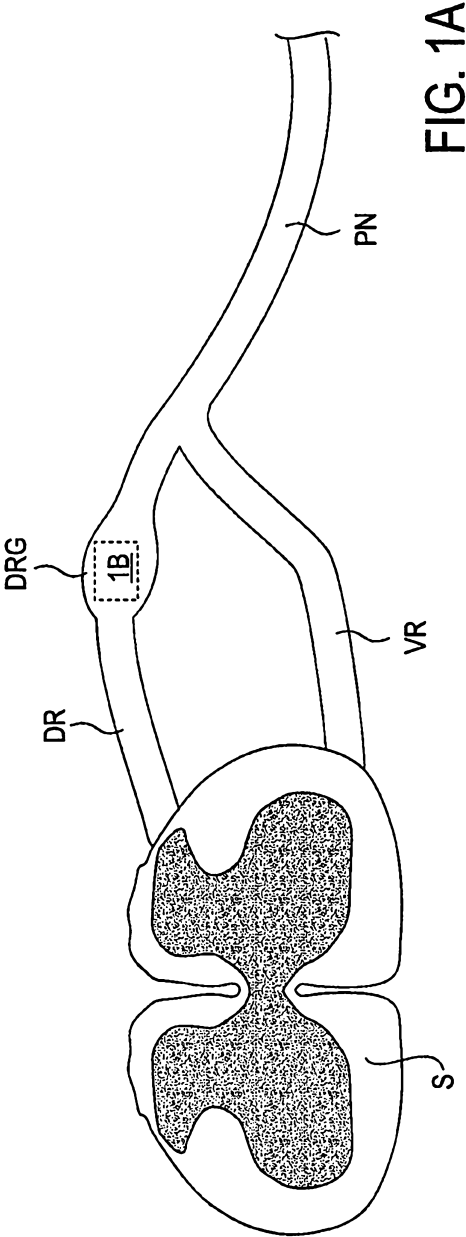


FIG. 1A

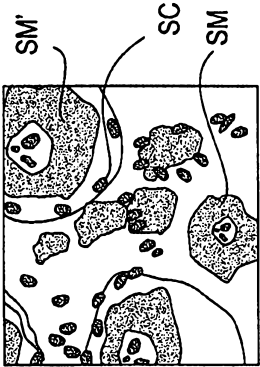


FIG. 1B



FIG. 2A



FIG. 2B

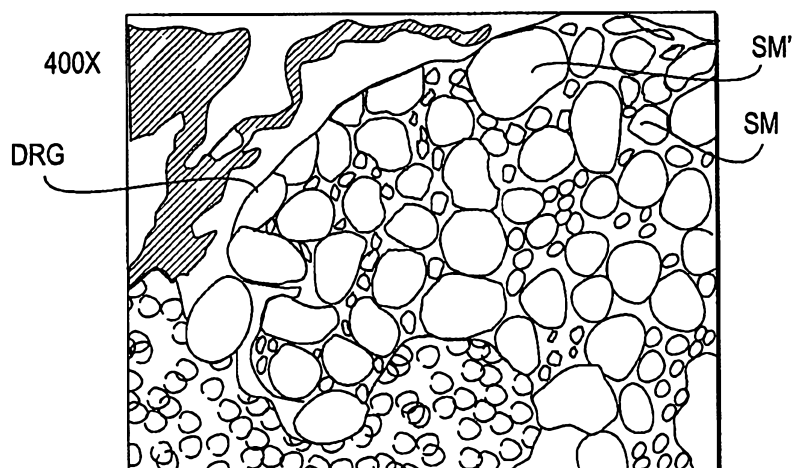


FIG. 2C

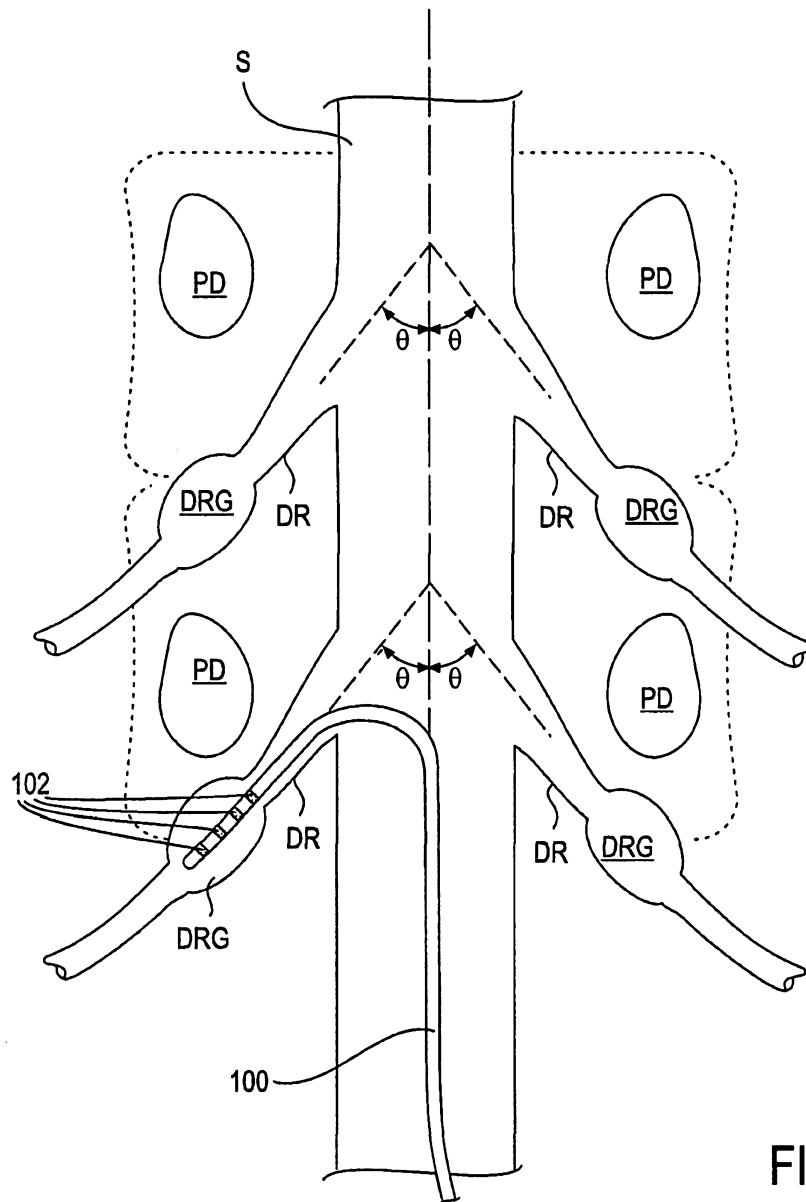


FIG. 3

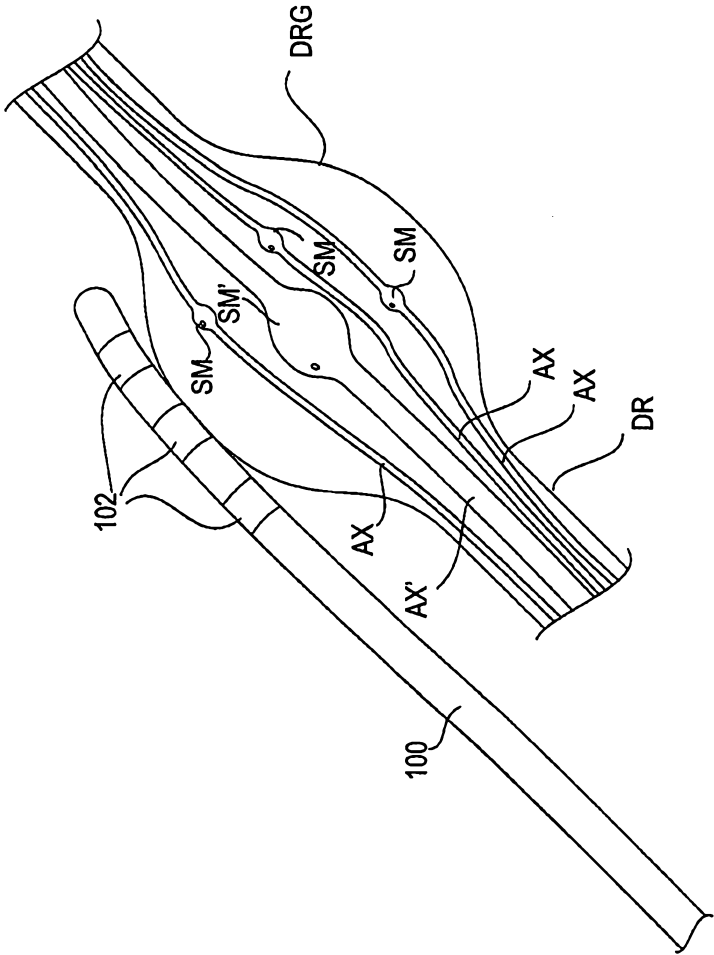


FIG. 4

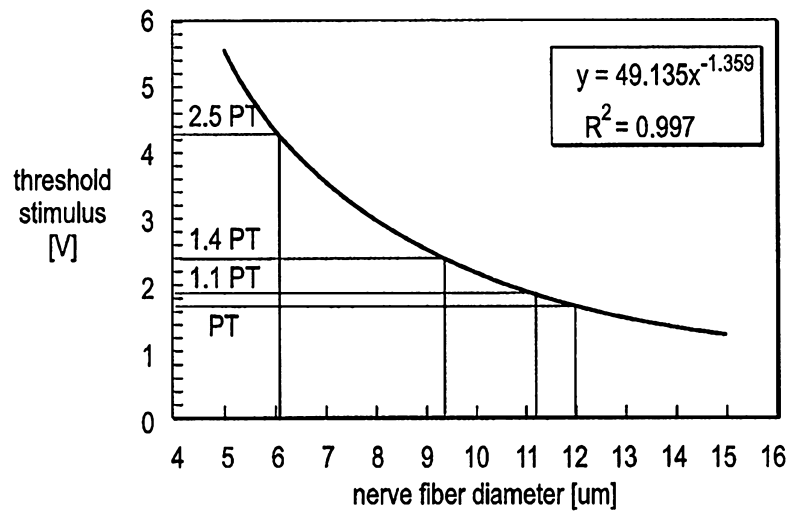


FIG. 5

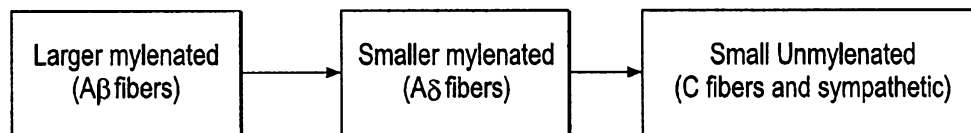


FIG. 6

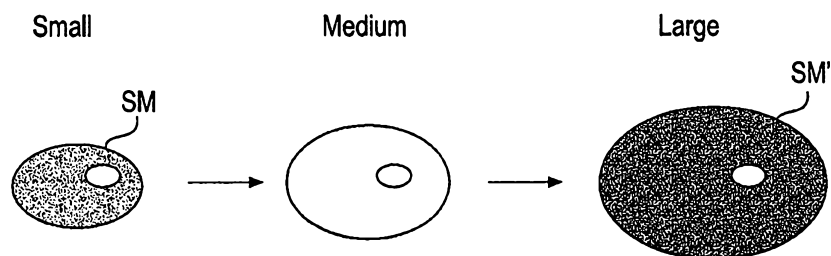


FIG. 7

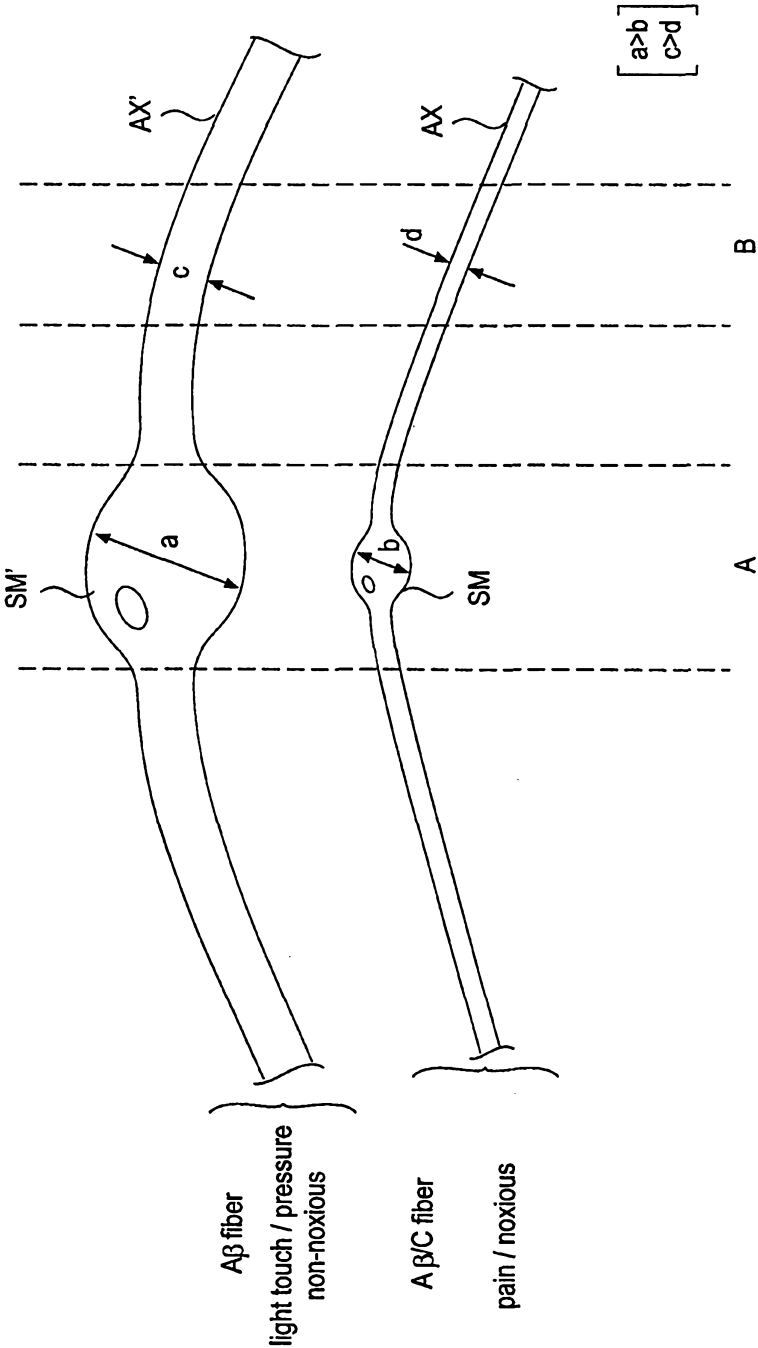


FIG. 8

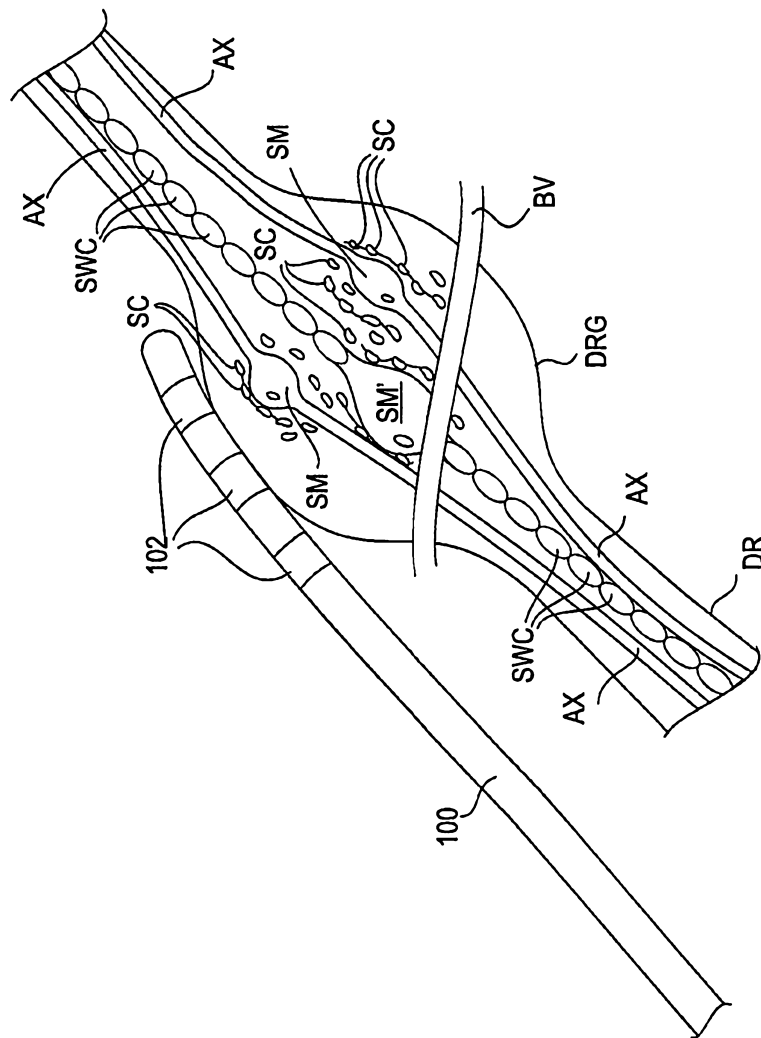


FIG. 9

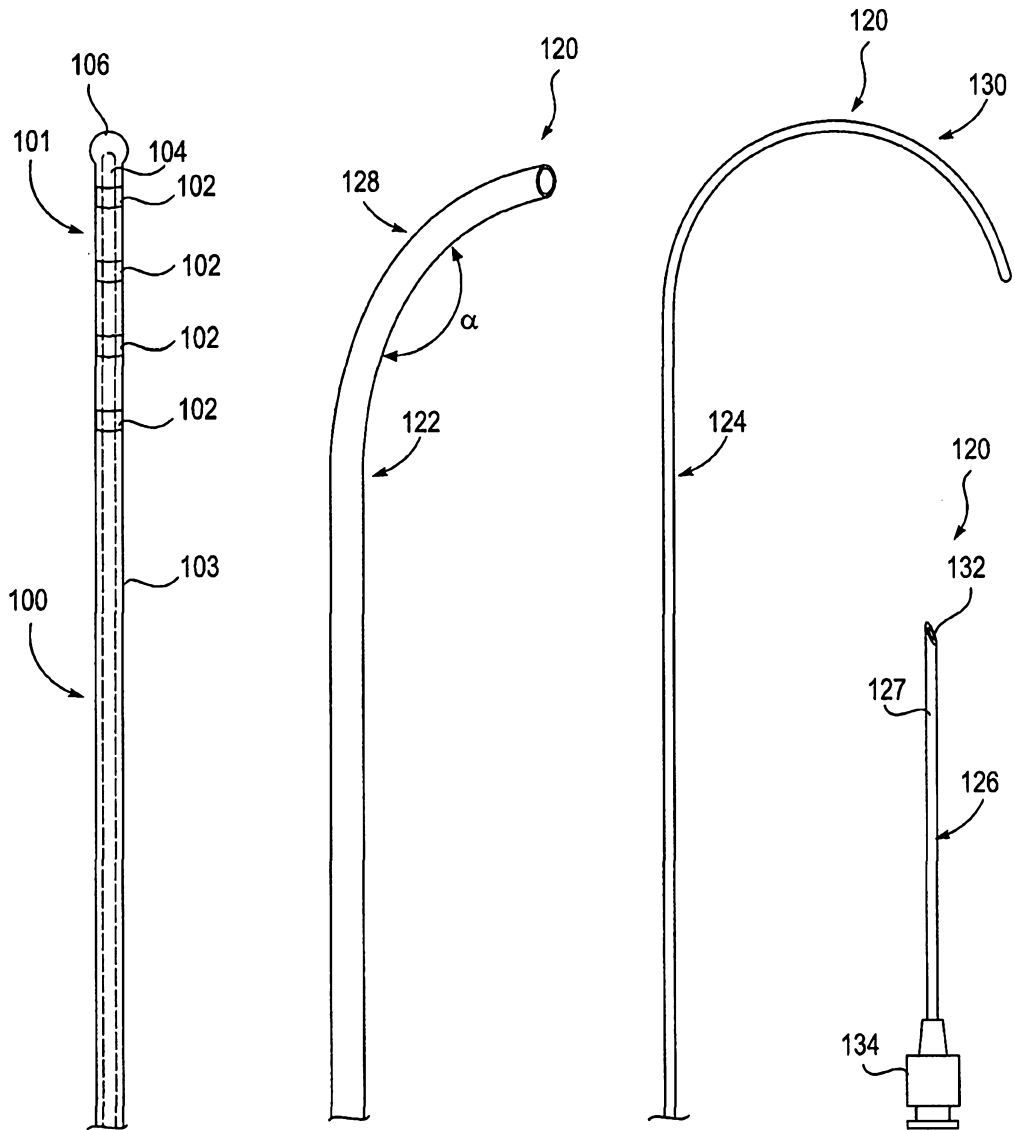


FIG. 10A

FIG. 10B

FIG. 10C

FIG. 10D

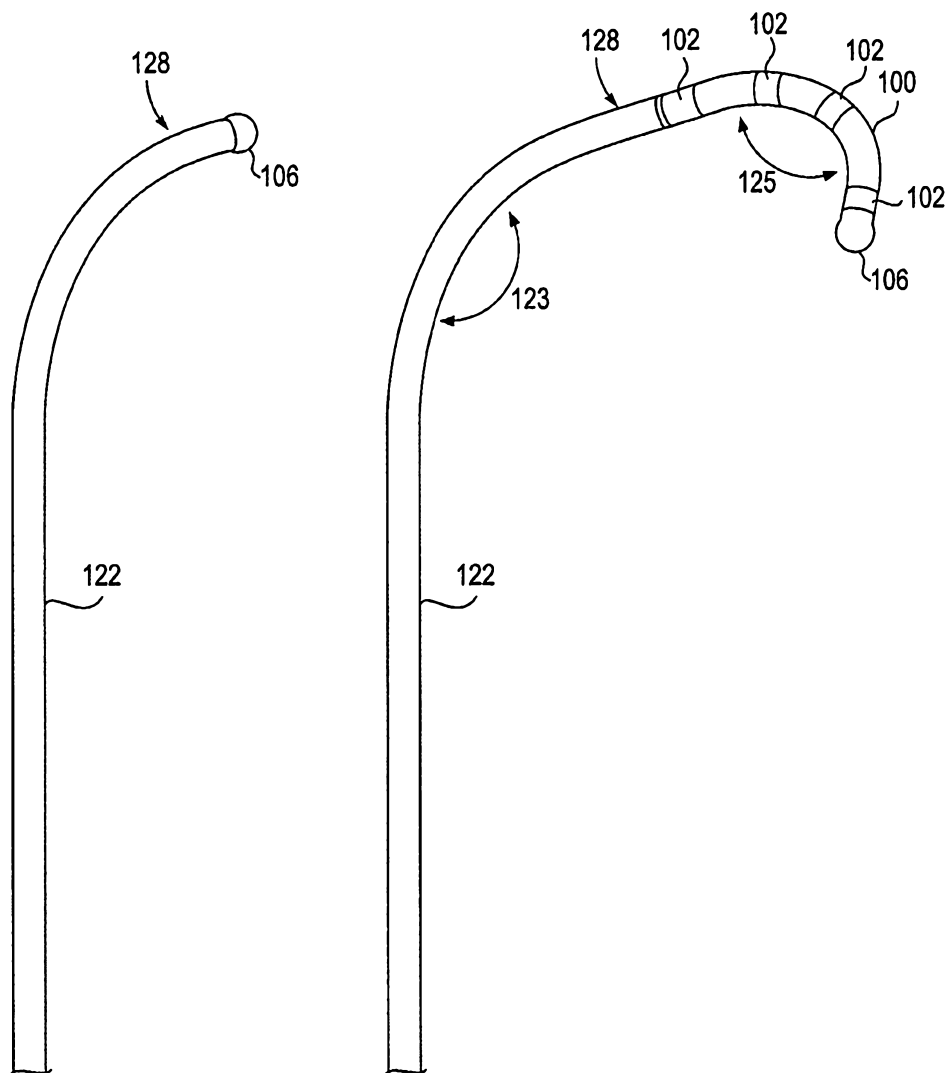


FIG. 11

FIG. 12