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(54) Title: SPINAL CORD STIMULATION FOR THE CONTROL OF CHRONIC ITCHING

(57) Abstract:

DESCRIPTION

SPINAL CORD STIMULATION FOR THE CONTROL OF CHRONIC ITCHING

[0001] The present application claims the priority benefit of United States provisional application number 61/776,524, filed March 11, 2013, the entire contents of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0002] The present invention relates generally to the field of neurostimulation. More particularly, it concerns the use of spinal cord stimulation to treat chronic pruritus.

2. Description of Related Art

[0003] Itching or pruritus is a common dermatological symptom that can give rise to considerable distress, in both humans and animals. Pruritus is often associated with inflammatory skin disease that can commonly be caused by hypersensitivity reactions (such as reaction to insect bites, *e.g.*, flea bites, or to environmental allergens, such as house dust mite or pollen), bacterial and fungal infections of the skin, or ectoparasite infections. Previous treatments for pruritus include the use of corticosteroids and antihistamines, however both have undesired side effects. Other therapies include the use of essential fatty acid dietary supplements which are slow to act and offer only limited efficacy against allergic dermatitis.

[0004] Chronic pruritus can be caused by burn injuries, chemotherapeutics, dermatologic and immunologic pathologies, and catastrophic injury. Current treatment of post burn pruritus involves symptomatic treatments using oral medications and topical preparations. The prevalence ranges from 93% to 73% from 6 months to 2 years after a burn injury (Carrougher *et al.*, 2012). Chronic post burn pruritus can lead to a limitation in vocational and recreational pursuits as well as a reduction in quality of life. Therefore, there is an unmet need for new and effective methods for treating chronic pruritus.

SUMMARY OF THE INVENTION

[0005] In a first embodiment of the present invention a method is provided for treatment pruritus in a patient, comprising electrically stimulating the spinal cord. Such methods can provide convenient, long-term management of chronic pruritus. In some aspects, electrical stimulation of the spinal cord can be performed by an implanted lead or leads that is in electrical communication with the patient's spinal cord. An implanted lead may comprise a plurality of electrodes, for example, 2, 3, 4, 5, 6, 7, 8, 16, or 32 electrodes. In order for a lead to be in electrical communication with the patient's spinal cord, it may be implanted, for example, into an epidural space or proximal to a dorsal root entry zone of the patient. In some aspects, stimulation over the dorsal root ganglia is contemplated. In some aspects, the epidural space may comprise any cervical, thoracic, lumbar, or sacral vertebral segment.

[0006] In a further aspect of the invention, the lead or leads is also in electrical communication with a medical device that can deliver electrical stimulation to the spinal cord *via* the lead or leads. For example, the medical device may be programmed to selectively deliver spinal cord stimulation in a manner and for a period of time sufficient to suppress pruritus. In another aspect, the medical device may deliver the stimulation based on a command received from the patient. In programming the medical device, various operating parameters for electrically stimulating the spinal cord can be selected. The optimal operating parameters may be selected by varying aspects of the electrical power generated by the medical device. The various aspects of the electrical power include, without limitation, the amplitude, pulse width, and frequency. The amplitude may vary between about 1 and about 15 V, preferably between about 0.1 and about 8 V, more preferably between about 0 and about 6 V, and most preferably between about 0 and about 4 V. The pulse width may vary between about 0 and about 1200 microseconds, preferably between about 0 and about 450 microseconds or between about 200 and about 500 microseconds, more preferably between about 180 and about 270 microseconds, and most preferably between about 240 and about 270 microseconds. The frequency may vary between about 10 and about 25,000 Hz, preferably between about 50 and about 3000 Hz, and more preferably between about 10 and about 350 Hz. Each of the operating parameters may be varied either alone or in combination with any other operating parameters. For example, the amplitude, pulse width, or frequency may be varied individually; the amplitude may be varied in combination with either the pulse

width or the frequency; the pulse width may be varied with the frequency; or all three may be varied in combination. An additional operating parameter may be optimized by, for example, applying electrical stimulation to different combinations of the plurality of electrodes.

[0007] In certain aspects, electrical stimulation may be used continuously or intermittently. It may be programmed at various pulse frequencies, widths, and amplitudes to achieve the desired effect of symptom reduction. It may also be beneficial if programmed such that the stimulation cycles change frequency, amplitude, and pulse width throughout the course of treatment.

[0008] In some aspects, a method of the embodiments further comprises diagnosing a subject with pruritus (*e.g.,* chronic pruritus) before treatment with the methods as described herein. Methods of diagnosing pruritus are well known in the art. In a related aspects, a method further comprises selecting a subject identified to have pruritus, such as chronic pruritus, before treatment with the methods as described herein.

[0009] Pruritus may be associated with any number of pathologic conditions including, for example, atopic dermatitis, psoriasis, chronic urticaria, HIV, herpetic neuralgia, chronic kidney disease, a hepatobiliary disease, or a hematopoietic disease. In one specific aspect, the chronic pruritus results from a burn. In still further aspects the pruritus may be associated with or a side effect of an anti-cancer therapy, such as chemotherapy or radiation therapy. In some aspects, a pruritus for treatment according to the embodiments is not associated with a burn.

[0010] In certain aspects a method of the embodiments further comprises monitoring the effect of the spinal cord stimulation on pruritus. This monitoring can be carried out using standard methods of measuring pruritus, including, for example, the 5-D Itch Scale, Leuven Itch Scale, and Itch Man Scale.

[0011] In a further embodiment, a method of treating pruritus in a patient comprises implanting a medical device for delivery of spinal cord stimulation to the patient, the stimulation being delivered *via* at least one lead comprised of at least two electrodes and the lead being implanted proximate to (*i.e.,* in electrical communication with) the spinal cord of the patient. Thus, once implanted, the electrical stimulation produced by operating the medical device, suppresses the pruritus.

[0012] In another embodiment, a method is provided of implanting a patient with a medical device capable of electrically stimulating the patient's spinal cord, wherein the patient is first identified as having pruritus, such as chronic pruritus.

[0013] In yet another embodiment, the present invention provides a method of treating a patient comprising selecting a patient comprising (1) an implant capable of electrically stimulating the patient's spinal cord and (2) having pruritus and programming or commanding the implant to provide an electrical stimulation in a manner sufficient to treat the pruritus.

[0014] As used herein the specification, "a" or "an" may mean one or more. As used herein in the claim(s), when used in conjunction with the word "comprising", the words "a" or "an" may mean one or more than one.

[0015] The use of the term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and "and/or." As used herein "another" may mean at least a second or more.

[0016] Throughout this application, the term "about" is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

[0017] Other objects, features and advantages of the present invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

I. Aspects of the Present Invention

[0018] Pruritus may become a chronic condition due to several etiologies. One common etiology of chronic, debilitating pruritus is seen in those patients who have suffered burn injuries. Other patients include those with dermatologic and immunologic pathologies.

At MD Anderson, patients undergoing chemotherapy and having burn injuries from radiation therapy may be at risk for chronic pruritus. The inventors have discovered a new application for spinal cord stimulation in providing a completely new way to treat chronic pruritus. Based on patient experience, spinal cord stimulation can be used to effectively treat chronic debilitating pruritus. Spinal cord stimulation may be the most meaningful treatment for chronic pruritus as a consequence of multiple etiologies.

II. Definitions

[0019] The term "pruritus" means itching, which can range from a mild sensation to an intense sensation.

[0020] The term "treating," as used herein, refers to altering the disease course of the subject being treated. Specifically, it refers to modulating certain areas of the spinal cord so that the subject has an improvement in the disease, for example, improvements in pruritus. Therapeutic effects of treatment include, without limitation, preventing occurrence or recurrence of disease, alleviation of symptom(s), diminishment of direct or indirect pathological consequences of the disease, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. One of skill in the art realizes that a treatment may improve the disease condition, but may not be a complete cure for the disease.

[0021] The terms "decrease," "reduce," "reduction," or "inhibit" are all used herein generally to mean a decrease by a significant amount. The significant amount may be a decrease by at least 5%, or by at least 10% as compared to a reference level, for example a decrease by at least about 5% or 10%, or about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90%, or up to and including a 100% decrease (*e.g.*, absent as compared to a reference level), or any decrease between 10%-100% as compared to a reference level.

[0022] The term "subject" is used interchangeably herein with "patient" and refers to a vertebrate, preferably a mammal, more preferably a primate, and still more preferably a human. A subject can be male or female. A subject can be one who has been previously diagnosed with or identified as suffering from a condition, such as chronic pruritus. A subject can also be one who is currently being treated for pruritus.

[0023] As used herein, "spinal cord," "spinal nervous tissue associated with a vertebral segment," "nervous tissue associated with a vertebral segment" or "spinal cord associated with a vertebral segment or level" includes any spinal nervous tissue associated with a vertebral level or segment. Those of skill in the art are aware that the spinal cord and tissue associated therewith are associated with cervical, thoracic, lumbar, and sacral vertebrae. As used herein, C1 refers to cervical vertebral segment 1, C2 refers to cervical vertebral segment 2, and so on. T1 refers to thoracic vertebral segment 1, T2 refers to thoracic vertebral segment 2, and so on. L1 refers to lumbar vertebral segment 1, L2 refers to lumbar vertebral segment 2, and so on. S1 refers to sacral vertebral segment 1, S2 refers to sacral vertebral segment 2, and so on, unless otherwise specifically noted. In certain cases, spinal cord nerve roots leave the bony spine at a vertebral level different from the vertebral segment with which the root is associated. For example, the T11 nerve root leaves the spinal cord myelum at an area located behind vertebral body T8-T9 but leaves the bony spine between T11 and T12.

[0024] As used herein, the use of the term "dorsal column" refers to conducting pathways in the spinal cord that are located in the dorsal portion of the spinal cord between the posterior horns, and which comprises afferent somatosensory neurons. The dorsal column is also known as the posterior funiculus.

[0025] As used herein, the use of the words "epidural space" or "spinal epidural space" is known to one with skill in the art, and refers to an area in the interval between the dural sheath and the wall of the spinal canal.

[0026] As used herein, the term "neuronal" refers to a neuron, which is a morphologic and functional unit of the brain, spinal column, and peripheral nervous system.

[0027] As used herein, the term "somatosensory system" refers to the peripheral nervous system division comprising primarily afferent somatic sensory neurons and afferent visceral sensory neurons that receive sensory information from skin and deep tissue, including the 12 cranial and 21 spinal nerves.

[0028] As used herein, the terms "stimulate" and "stimulation" refer to electrical stimulation that modulates predetermined sites in the nervous system.

[0029] As used herein, the terms "spike," "action potential," and "pulse" all refer to a rapid rise and fall of voltage in a specified region of space. One skilled in the art realizes that the term action potential generally refers to a spike or pulse that is produced by a neuron. One skilled in the art also recognizes that the term action potential can also be expanded to include the spiking of cells in other excitable tissues. The terms spike and pulse may refer to action potentials produced by neurons and other excitable cells and may also refer to artificial stimulations that mimic the features of action potentials in cells or groups of cells. The terms "inter-spike interval" or "inter-pulse interval" refer to the period of time between two action potentials, spikes, or pulses. However, one of skill in the art also realizes that naturally occurring spikes do not necessarily occur at a fixed rate; this rate can be variable. In such cases an average inter-spike interval may be used to define the average period of time between consecutive action potentials, spikes, or pulses in a series.

[0030] As used herein, the term "burst" refers to a rapid succession of two or more neuronal action potentials or external stimuli in the approximate frequency range of 50-1000 Hz (Beurrier *et al.*, 1999) that, possibly, occurs during a plateau or active phase, followed by a period of relative quiescence called the silent phase (Nunemaker and Satin, 2005). A burst stimulation may occur from a plateau or elevated pulse amplitude applied by the pulse stimulator. Also, a hyper-polarizing or other pre-conditioning pulse may precede the burst. A charge balancing pulse or pulses may be applied within the burst or at the end of the burst. A burst spike may be described as a spike that is preceded or followed by another spike within a short time interval of approximately (0.1-10 msec) (Matveev, 2000). Those skilled in the art recognize that a burst can refer to a plurality of groups of spike pulses. In some embodiments, a burst may be a period in time in which two or more spikes occur relatively rapidly, such that the spikes summate in the dendrites or cell body of a neuron in a non-linear fashion. The period of time between the beginning of a burst and the end of the same said burst is the "intra-burst interval." The period of time between two bursts is the "inter-burst interval." For example, 1 milliseconds to about 5 seconds, more preferably, about 10 milliseconds to about 300 milliseconds. In some embodiments, the burst stimulus may comprise pulse amplitude ramping, for example increasing the amplitude of successive pulses within an individual burst. One skilled in the art is also aware that burst firing can also be referred to as phasic firing, rhythmic firing (Lee *et al.*, 2001), pulse train firing, oscillatory firing, and spike train firing, all of these terms used herein are interchangeable.

[0031] As used herein, the term "tonic" as well as the phrases "tonic firing," "tonic spike," "tonic pulse," or "tonic mode" refers to any process in which the firing pattern can be accurately described as a series of single spikes of a given frequency or with a given inter-spike interval, wherein the inter-spike interval may be fixed or variable.

III. Pruritus

[0032] Itching or pruritus is a common dermatological symptom that can give rise to considerable distress, in both humans and animals.

[0033] Pruritus can originate in the peripheral nervous system (*i.e.*, dermal or neuropathic) or in the central nervous system (*i.e.*, neuropathic, neurogenic, or psychogenic). The numerous causes of pruritus include atopic dermatitis, psoriasis, chronic urticaria, post-burn healing, chronic *kidney* disease, hapatobiliary diseases, HIV, and hematopoietic diseases (Tivoli *et al.*, 2009; Goutos *et al.*, 2010).

[0034] Several clinical tools are available to assess and quantify pruritus. These include the Itch Man Scale (Blakeney and Marvin, 2000; Morris *et al.*, 2012), the Leuven Itch Scale (Haest *et al.*, 2011), and the 5-D itch scale (Elman *et al.*, 2010).

IV. Spinal Cord Stimulation

[0035] Spinal cord stimulation (SCS) involves stimulating the spinal cord at specifically targeted locations, typically via leads and electrodes that are either surgically implanted post laminectomy or inserted percutaneously and are connected to a power source to enable conduction of electrical impulses to the spinal cord. Delivering stimulation to the appropriate location on the spinal cord causes paresthesia, which may be experienced by the patient in a relatively large area, including more than one limb. Electrodes for SCS may be implanted in the epidural space near vertebral levels T8-T10 to treat the axial region of the back, over the dorsal columns at vertebral levels T10-L1 to treat pain in the back, legs, ankles, or feet, or over the dorsal root of vertebral levels L3-S1. Electrodes may stimulate either the dorsal column or the dorsal root ganglia. The number of leads implanted ranges from one lead to ten leads. Preferably, the number of leads implanted ranges from one lead to four leads. More preferably, the number of leads implanted ranges from one lead to two leads. Most preferably, the number of leads implanted is two.

[0036] Preferably, the lead or leads are inserted into the epidural space of the spinal cord and contact the external portion of the dura to stimulate the neural structures underneath. The lead or leads may be inserted into the sacral, lumbar, thoracic, or cervical vertebral regions. The position of the implanted lead or leads ranges from the sacral position to the high cervical position of the spinal cord. Preferably, the lead or leads are implanted from the upper lumbar to the lower cervical position in the spinal cord. More preferably, the lead or leads are implanted from the lower thoracic to the higher thoracic position of the spinal cord. Most preferably, the lead or leads are implanted from the lower thoracic to the middle thoracic position in the spinal cord. The lead or leads are positioned so that the lead or leads are parallel to the midline of the spinal cord and may be positioned to the right of the midline, directly on the midline or to the left of the midline. The lead or leads may also be placed oblique or transverse to the midline. If more than one lead is implanted, the leads may be positioned both to the right and left of the midline of the spinal cord.

[0037] Conventional neuromodulation devices typically include a microprocessor and a pulse generation module. The pulse generation module generates the electrical pulses according to a defined pulse width and pulse amplitude and applies the electrical pulses to defined electrodes. The microprocessor controls the operations of the pulse generation module according to software instructions stored in the device. In one embodiment of the invention, stimulation systems that combine a pulse generator and electrodes for tissue stimulation in a single system may be used. Alternatively, in another embodiment, a stimulation system with flexible leads is also contemplated. One with skill in the art realizes that the methods of the present invention are appropriate for use with any stimulation device capable of providing stimulation to spinal nervous tissue.

[0038] Exemplary devices compatible with use with the present invention include, but are not limited to, the RestoreSensor, RestoreUltra, RestoreAdvanced, RestorePrime, PrimeAdvanced, and Itrel neurostimulators (Medtronic); the Precision Plus SCS System (Boston Scientific); and the Eon Mini (St. Jude Medical). The devices listed herein are not meant to limit the scope of the invention in any way; any device or system component that performs an equivalent function is also contemplated. For example, see U.S. Patent Nos. 4,379,462; 5,417,719; 5,501,703; 5,643,330; 6,120,467; 6,440,090; 6,516,227; 6,675,046; 6,871,099; 6,895,280; 7,496,404; and 7,610,102 and U.S. Pat. Publn. Nos. 20020111661 and 20040167584, each of which is incorporated herein, in its entirety, by reference.

[0039] The preferred neurostimulation devices should allow each electrode of each lead to be defined as a positive, a negative, or a neutral polarity. In current technology, a lead can have anywhere from four to eight to sixteen to thirty-two electrode contacts. Different electrodes on the lead can be selected by suitable computer programming, such as that described in U.S. Pat. No. 5,938,690, which is incorporated herein by reference in its entirety. For each electrode combination (*e.g.*, the defined polarity of at least two electrodes having at least one cathode and at least one anode), an electrical signal can have at least a definable amplitude (*e.g.*, voltage), pulse width, and frequency, where these variables may be independently adjusted to finely select the sensory transmitting nerve tissue required to inhibit transmission of neuronal signals. Generally, amplitudes, pulse widths, and frequencies are determinable by the capabilities of the neurostimulation systems, which are known by those of skill in the art.

[0040] For example, the amplitude of the electrical power may be varied between about zero volts to about fifteen volts and is chosen to be as high as can be tolerated by the patient so as to achieve maximum stimulation. Preferably, the voltage is varied between about 0.1 volts to about eight volts. More preferably, the voltage is varied between about zero volts to about six volts and most preferably, the voltage is varied between about zero to about four volts. The pulse width of the electrical power may also be varied at the same time as one or more of the characteristics of the electrical power or may be separately varied with the other characteristics held constant. Preferably, the pulse width is varied between about zero to about 1200 microseconds. More preferably, the pulse width is varied between about zero to about 450 microseconds, between about 200 to about 500 microseconds, or between about 180 to about 270 microseconds. Most preferably, the pulse width is varied between about 240 to about 270 microseconds. The rate of the electrical power may also be varied at the same time as one or more of the characteristics of the electrical power or may be separately varied with the other characteristics held constant. Preferably, the rate is varied between about zero to about 150 cps. More preferably, the rate is varied between about 25 to about 80 cps and most preferably, the rate is varied between about 50 to about 80 cps. Signal frequencies may be between 10-25,000 Hz, and in one embodiment approximately 50-3,000 Hz, and in a preferred embodiment between 10-350 Hz.

V. Examples

[0041] The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

Example 1 – Spinal cord stimulation to treat pruritus – patient one

[0042] The inventors performed spinal cord stimulation on a patient for an FDA approved indication (pain). The inventors discovered that stimulation of the dorsal columns also provided profound reduction in the patient's pruritus.

[0043] The patient was a mid-fifties year old man with a 50%-60% total body surface area burn on his lower body. Approximately 25% was third degree burns. The patient previously required multiple skin grafts to cover the burned areas. The inventors evaluated him for management of neuropathic pain in the areas of burn injury and skin grafting. He had severe pain in the bilateral anterior thighs and bilateral posterior popliteal regions. He was treated with pharmacologic therapy that was standard of care for his chronic pain issues from the burn injuries. The focus of treatment was for neuropathic pain. Pruritus at the area of the burn injury was a collateral symptom he complained of during our evaluation. Pruritus was limiting his quality of life, but was not initially the focus of our treatment.

[0044] Functionally, the pain produced significant interference with general activity, normal work, mood, relationships, sleep, and enjoyment of life. On physical examination, the patient had normal muscle strength and reflexes in the lower extremities. The skin on his anterior thighs and popliteal spaces showed extensive areas of hypertrophic scarring secondary to skin grafting. He had significant allodynia at the transition sites from hypertrophic scars to normal skin. These transition sites are the same regions that the patient reported both neuropathic pain and pruritus.

[0045] The patient's initial management included optimization of pharmacologic therapy. Gabapentin and Duloxetine were continued. In addition, the inventors initiated a neuropathic cream for him to apply to painful areas. The inventors also offered him a trial of spinal cord stimulation for his lower extremity neuropathic pain, but the inventors were also interested with the potential effect for his chronic pruritus.

[0046] The inventors performed a percutaneous trial of spinal cord stimulation using two Medtronic Octrodes leads over the superior portion of the T8 vertebral level in a standard fashion. Participation of a Medtronic representative was standard for both trial and implantation of SCS. Coverage of all painful areas with comfortable paresthesias is the goal of SCS and this was achieved without difficulty.

[0047] The outcome of the SCS trial was favorable for the control of pain. The patient reported that it also controlled his chronic pruritus.

[0048] The inventors subsequently implanted the following permanent devices after the successful trial:

1. Medtronic 3777-60 lead
2. Medtronic 3777-60 lead
3. RestoreSensor internal pulsed generator
4. Medtronic Titan anchors 3550-39.

[0049] Subsequent follow-up after implantation resulted in continued patient reports of reduction in both pain and pruritus.

Example 2 – Spinal cord stimulation to treat pruritus – patient two

[0050] The inventors performed spinal cord stimulation on a patient for an FDA approved indication (pain). The patient was a 31-year-old female with no past medical history. She sustained an auto-pedestrian accident resulting in an above-the-elbow left upper extremity amputation with multiple revisions and skin grafting. She required a left chest latissimus dorsi flap.

[0051] The patient was evaluated for pain control at the site of the stump and adhesive capsulitis with complex regional pain syndrome. Pharmacologic therapy, stellate ganglion blocks and rehabilitation provided marginal reduction in pain.

[0052] Spinal cord stimulation (cervical lead placement) was performed with a reduction in pain. A Boston Scientific precision Spectra Internal pulse generator was implanted with two Boston Scientific, 16-contact Infinion leads placed at the left dorsal column of the C2-C6 vertebral levels and left C2 neuralforamen to C6 lateral recess.

[0053] One month after implantation, the patient reported chronic pruritis of her left chest wall at the area of the graft site. She had no complaints of pain at the chest area, just pruritis. This symptom was previously unreported. Reprogramming of the stimulator to provide paresthesias over that area provided her with 100% resolution of her chronic pruritis.

* * *

[0054] All of the methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

REFERENCES

The following references, to the extent that they provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference.

U.S. Patent 4,379,462

U.S. Patent 5,417,719

U.S. Patent 5,501,703

U.S. Patent 5,643,330

U.S. Patent 6,120,467

U.S. Patent 6,440,090

U.S. Patent 6,516,227

U.S. Patent 6,675,046

U.S. Patent 6,871,099

U.S. Patent 6,895,280

U.S. Patent 7,496,404

U.S. Patent 7,610,102

U.S. Pat. Publn. No. 20020111661

U.S. Pat. Publn. No. 20040167584

Beurrier *et al.*, Subthalamic nucleus neurons switch from single-spike activity to burst-firing mode, *J. Neurosci.*, 19(2):599-609, 1999.

Blakeney and Marvin, Itch man scale, Copyrighted by Shriners Hospitals for Children, 2000.

Carrougher *et al.*, Pruritus in adult burn survivors: postburn prevalence and risk factors associated with increased intensity, *J. Burn Care Res.*, Vol, Pg, 2012.

Elman *et al.*, The 5-D itch scale: a new measure of pruritus, *Br. J. Dermatol.*, 162:587-593, 2010.

Goutos *et al.*, Review of therapeutic agents for burns pruritus and protocols for management in adult and paediatric patients using the GRADE classification, *Indian J. Plast. Surg.*, 43(suppl):S51-S62, 2010.

Haest *et al.*, Measurement of itching: validation of the Leuven Itch Scale, *Burns*, 37:939-950, 2011.

Lee *et al.*, Discharge profiles of ventral tegmental area GABA neurons during movement, anesthesia, and the sleep-wake cycle, *J. Neurosci.*, 21(5):1757-66, 2001.

Matveev, Differential short-term synaptic plasticity and transmission of complex spike trains: to depress or to facilitate, *Cerebral Cortex*, 10(11):1143-1153, 2000.

Morris *et al.*, Itch assessment scale for the pediatric burn survivor, *J. Burn Care Res.*, 33:419-424, 2012.

Nunemaker and Satin, A tale of two rhythms: a comparative review of the pulsatile endocrine systems regulating insulin and GnRH secretion, *Cellscience Reviews*, 2(1):92-126, 2005.

Tivoli *et al.*, Pruritus: An updated look at an old problem, *J. Clin. Aesthetic Dermatol.*, 2(7):30-36, 2009.

CLAIMS

1. A method of treating pruritus in a patient in need thereof, comprising applying electrical stimulation to the spinal cord of the patient in a manner sufficient to effectively treat the pruritus.

2. The method of claim 1, wherein electrically stimulating the spinal cord of the patient comprises delivering spinal cord stimulation via at least one lead implanted in electrical communication with the spinal cord of the patient.

3. The method of claim 2, wherein the lead is implanted in an epidural space or proximal to a dorsal root entry zone of the patient.

4. The method of claim 2, wherein the at least one lead comprises a plurality of electrodes.

5. The method of claim 3, wherein the epidural space comprises a cervical vertebral segment.

6. The method of claim 3, wherein the epidural space comprises a thoracic vertebral segment.

7. The method of claim 3, wherein the epidural space comprises a lumbar vertebral segment.

8. The method of claim 3, wherein the epidural space comprises a sacral vertebral segment.

9. The method of claim 2, wherein the lead is in electrical communication with a medical device such that the device can deliver spinal cord stimulation via the at least one lead.

10. The method of claim 9, wherein the medical device selectively delivers the spinal cord stimulation in a manner and for a period of time sufficient to suppress said pruritus.

11. The method of claim 9, wherein the medical device selectively delivers the spinal cord stimulation based on a command received from the patient or a schedule.

12. The method of claim 1, further comprising selecting the optimal operating parameters for electrically stimulating the spinal cord from a plurality of operating parameters.

13. The method of claim 12, wherein selecting the optimal operating parameters comprises applying electrical stimulation to different combinations of the plurality of electrodes and varying at least one aspect of the electrical power generated by the medical device.

14. The method of claim 13, wherein the one aspect of the electrical power that is varied is amplitude.

15. The method of claim 13, wherein the one aspect of the electrical power that is varied is pulse width.

16. The method of claim 13, wherein the one aspect of the electrical power that is varied is frequency.

17. The method of claim 13, further comprising monitoring the effect of the spinal cord stimulation on the pruritus.

18. The method of claim 17, wherein monitoring comprises administering the 5-D Itch Scale, Leuven Itch Scale, or Itch Man Scale.

19. The method of claim 1, wherein stimulating the spinal cord comprises delivering electrical pulses on a substantially continuous basis.

20. The method of claim 1, wherein the pruritus results from atopic dermatitis, psoriasis, chronic urticaria, HIV, herpetic neuralgia, chronic kidney disease, a hepatobiliary disease, or a hematopoietic disease.

21. The method of claim 1, wherein the pruritus results from a burn.

22. A method of treating pruritus in a patient, comprising (a) implanting a medical device that delivers spinal cord stimulation to the patient via at least one lead comprised of two electrodes implanted in electrical communication with the spinal cord of the patient, (b) electrically stimulating the spinal cord by operating the medical device, and (c) suppressing the pruritus with the stimulation.

23. A method of implanting a patient, comprising (a) identifying a patient having pruritus, and (b) implanting a medical device capable of electrically stimulating the patient's spinal cord.

24. A method of treating pruritus comprising (a) identifying a patient having pruritus and comprising an implant capable of electrically stimulating the patient's spinal cord, and (b) programming or providing command to said implant in a manner sufficient to treat the pruritus.

PATENT COOPERATION TREATY

PCT

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

(PCT Article 17(2)(a), Rules 13*ter*.1(c) and (d) and 39)

Applicant's or agent's file reference	**IMPORTANT DECLARATION**	Date of mailing (*day/month/year*)
UTFC.P1205WO		01 July 2014 (01.07.2014)
International application No.	International filing date (*day/month/year*)	(Earliest) Priority date (*day/month/year*)
PCT/US2014/023413	**11 March 2014 (11.03.2014)**	11 March 2013 (11.03.2013)

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

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

Applicant

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM

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. ☒ 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. ☒ methods for treatment of the human body by surgery or therapy
   - j. ☐ methods for treatment of the animal body by surgery or therapy
   - k. ☐ diagnostic methods practised on the human or animal body
   - l. ☐ mere presentation 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:

   ☐ the description ☐ the claims ☐ the drawings
3. ☐ A meaningful search could not be carried out without the sequence listing; the applicant did not, within the prescribed time limit:
   - ☐ 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.
   - ☐ 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.
   - ☐ 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. Further coments:

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