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(54) **SYSTEMS AND METHODS TO PLACE ONE OR MORE LEADS IN TISSUE FOR PROVIDING FUNCTIONAL AND/OR THERAPEUTIC STIMULATION**

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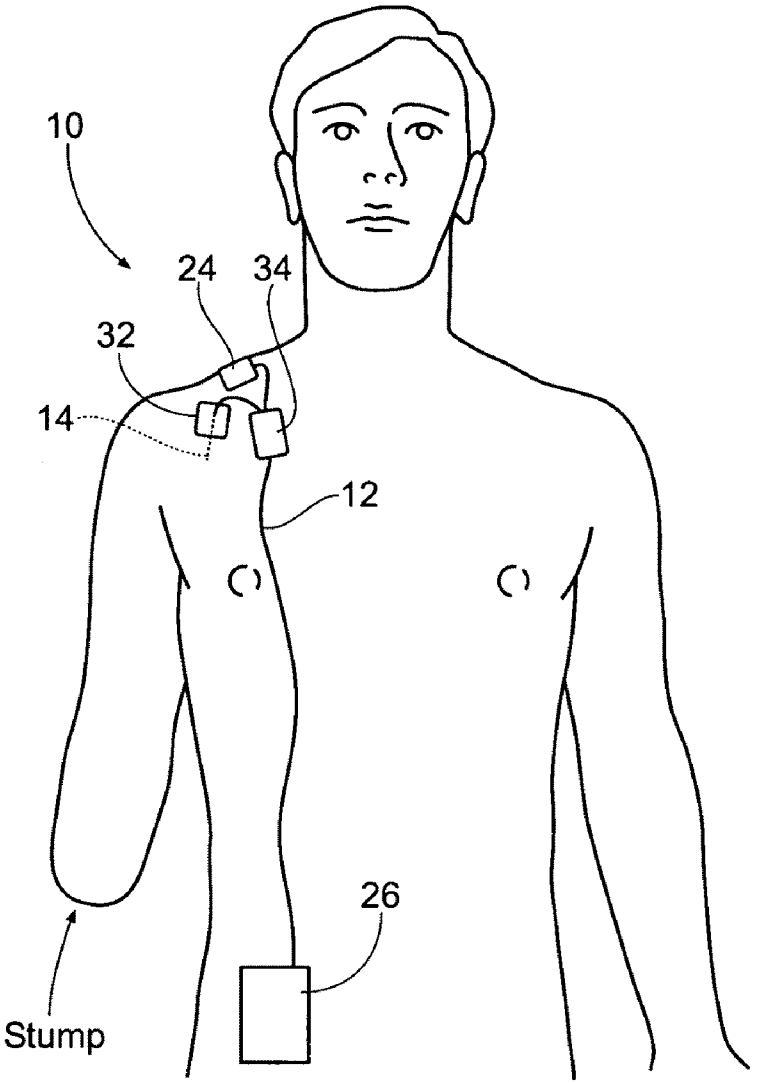
(57) **ABSTRACT**

Systems and methods make possible the placement of one or more electrode leads in a tissue region for providing functional and/or therapeutic stimulation to tissue. The systems and methods are adapted to provide the relief of pain.



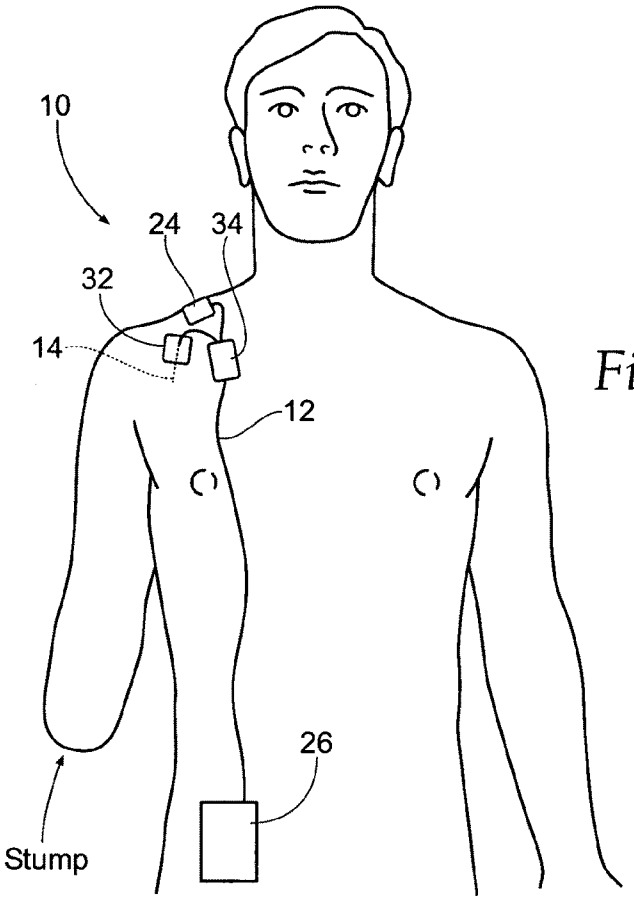


Fig. 1

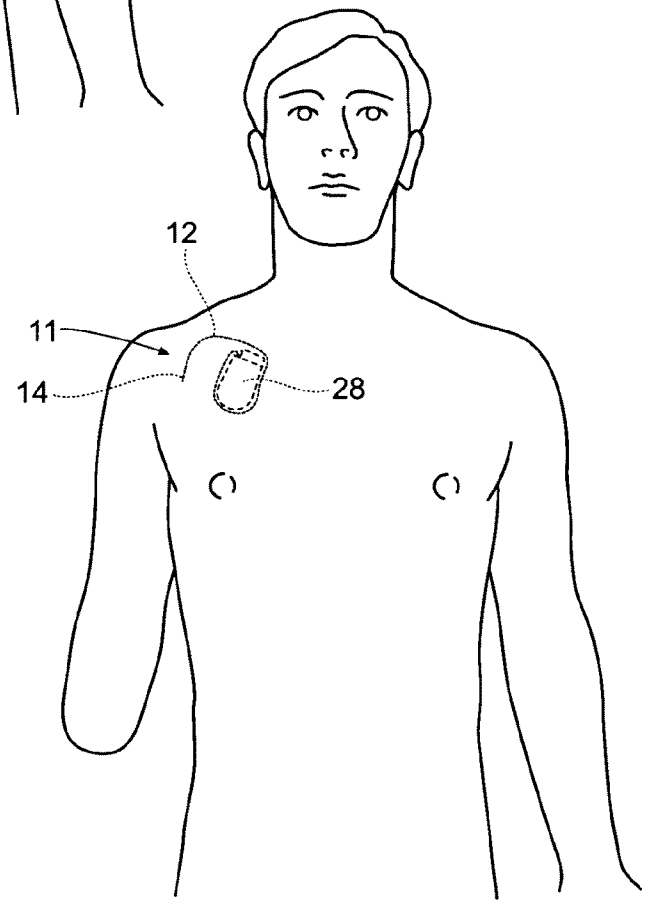


Fig. 2

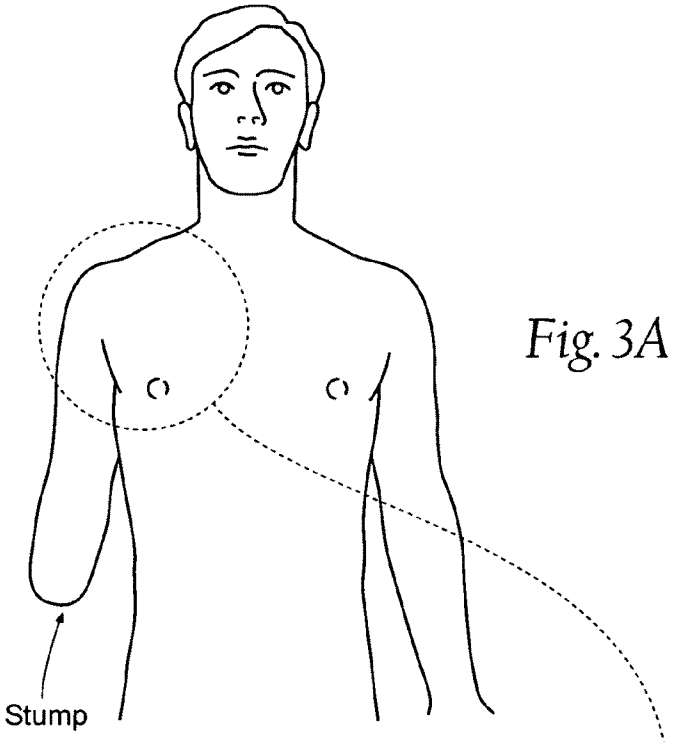


Fig. 3A

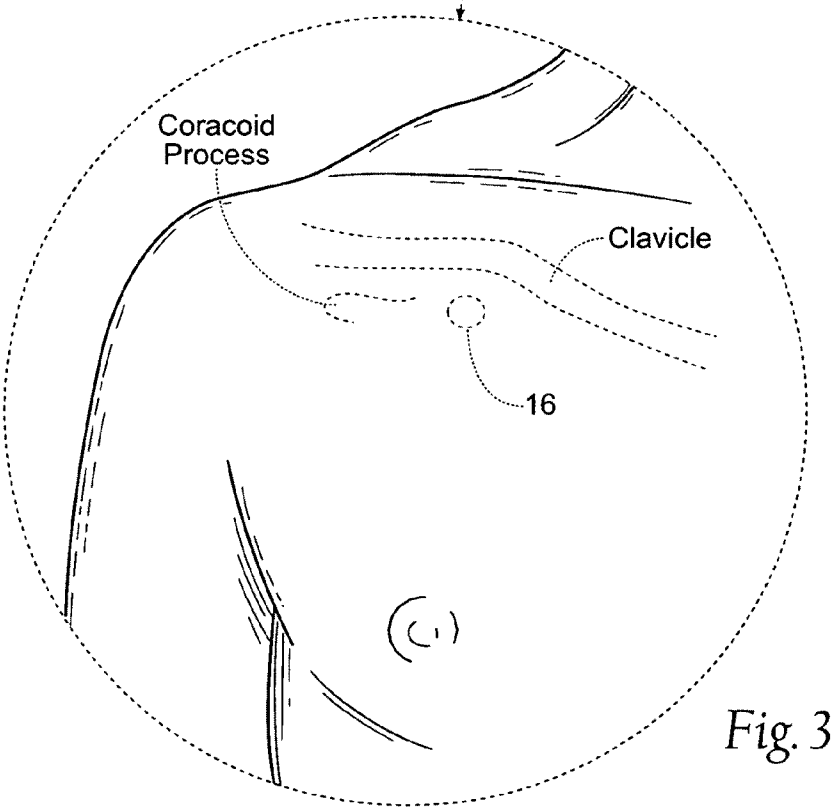


Fig. 3B

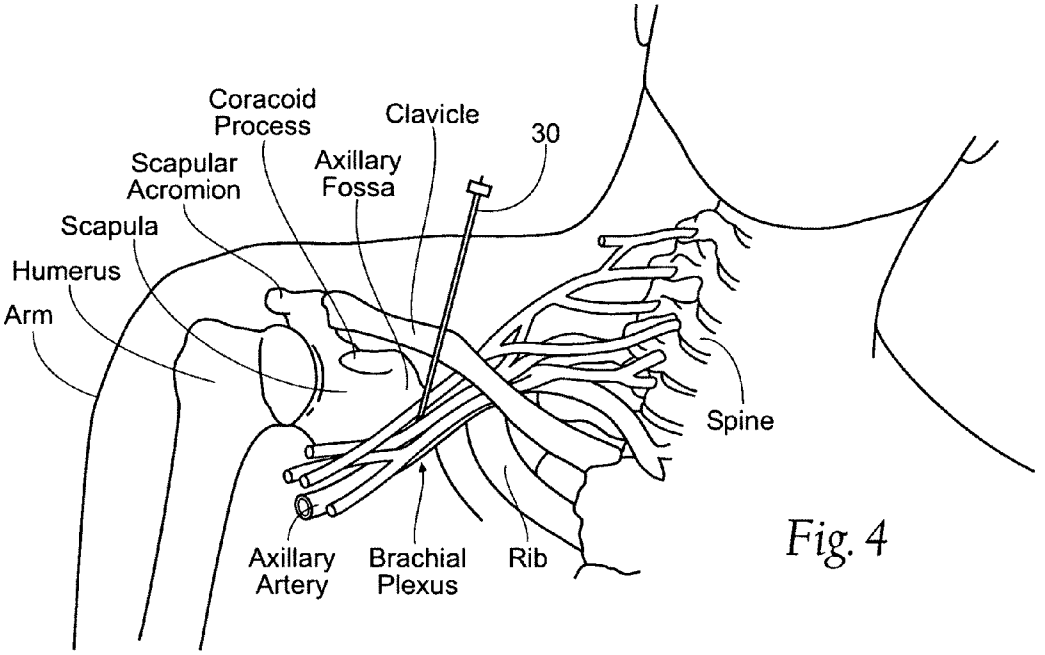

Coracoid Process
Clavicle
30
Scapular Acromion
Axillary Fossa
Scapula
Humerus
Arm
Spine
Axillary Artery
Brachial Plexus
Rib

Fig. 4

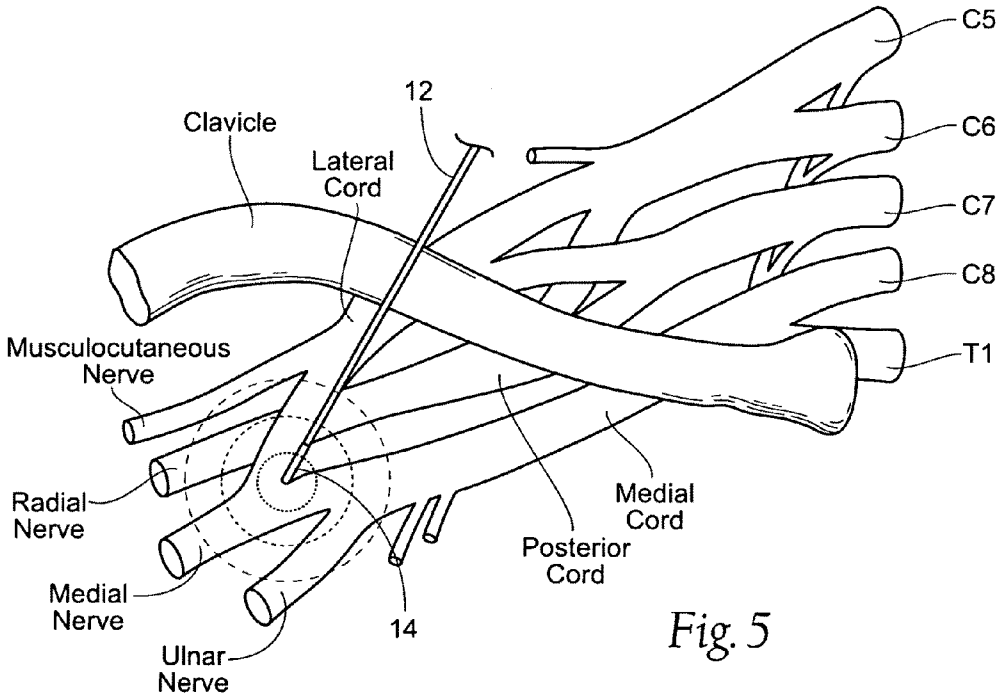

C5
12
Clavicle
C6
Lateral Cord
C7
C8
T1
Musculocutaneous Nerve
Radial Nerve
Medial Cord
Posterior Cord
Medial Nerve
14
Ulnar Nerve

Fig. 5

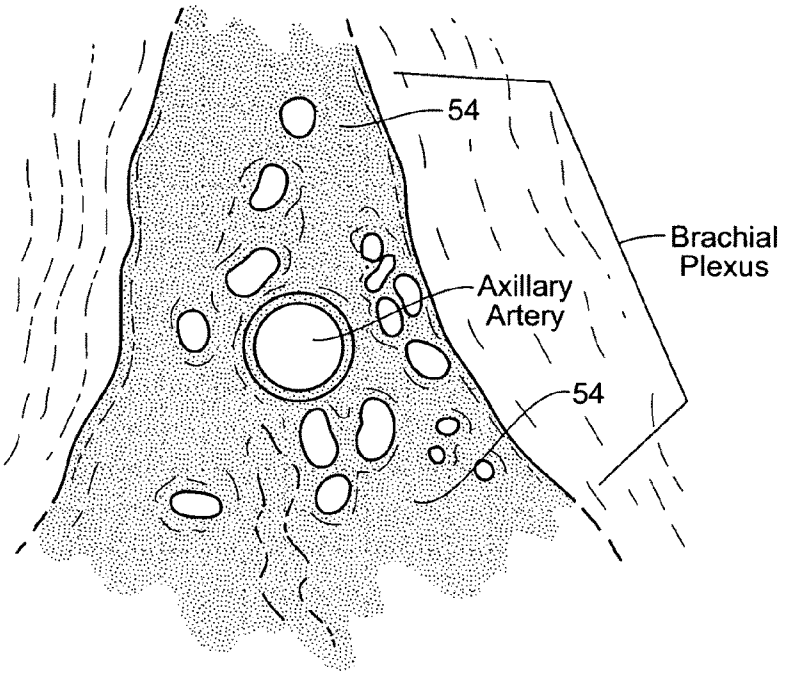

54
Brachial Plexus
Axillary Artery
54

Fig. 6

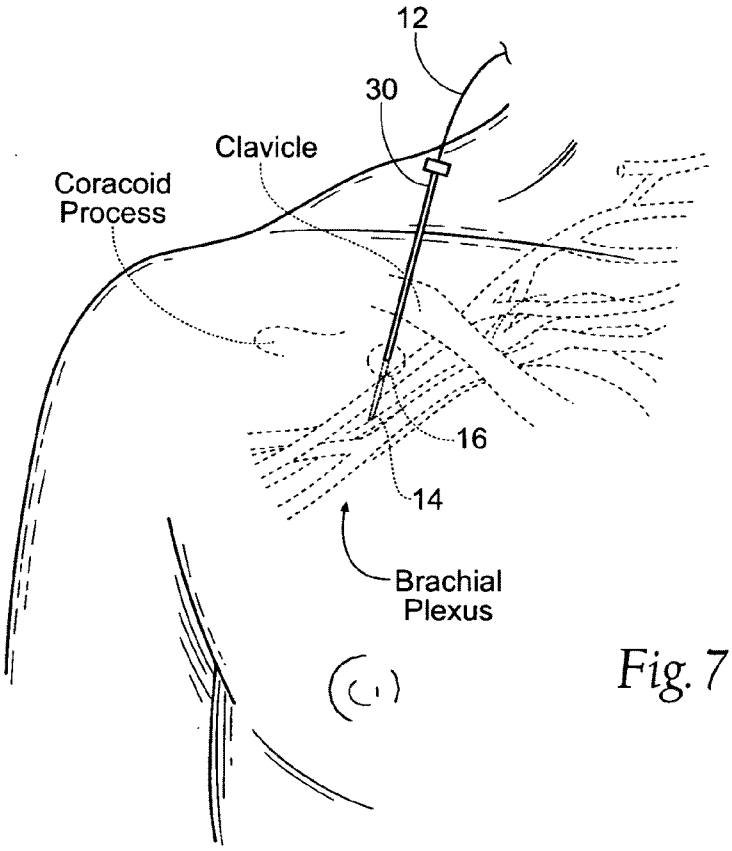

12
30
Clavicle
Coracoid Process
16
14
Brachial Plexus

Fig. 7

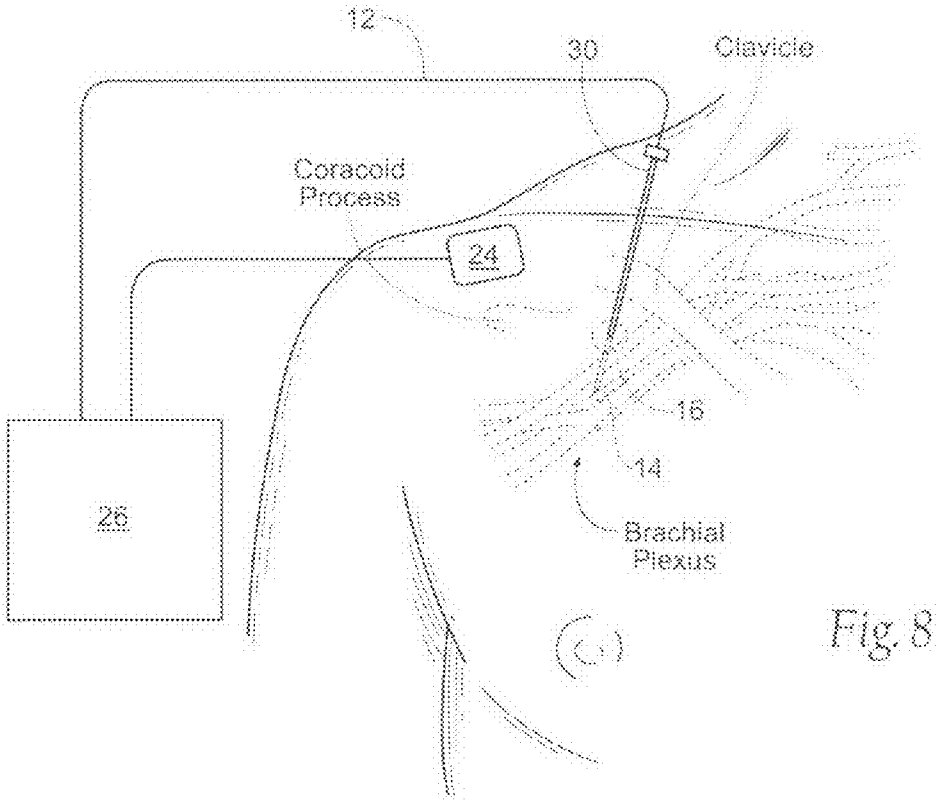


Fig. 8

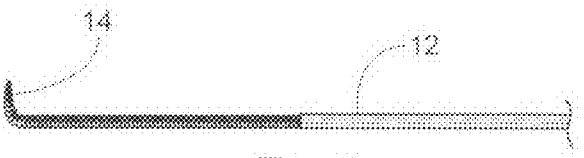


Fig. 9

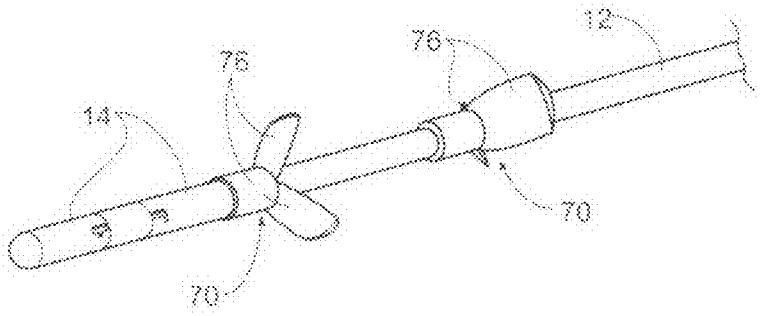


Fig. 10

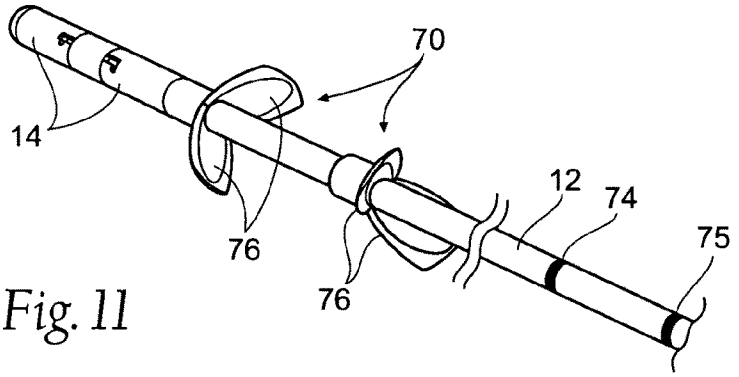


Fig. 11

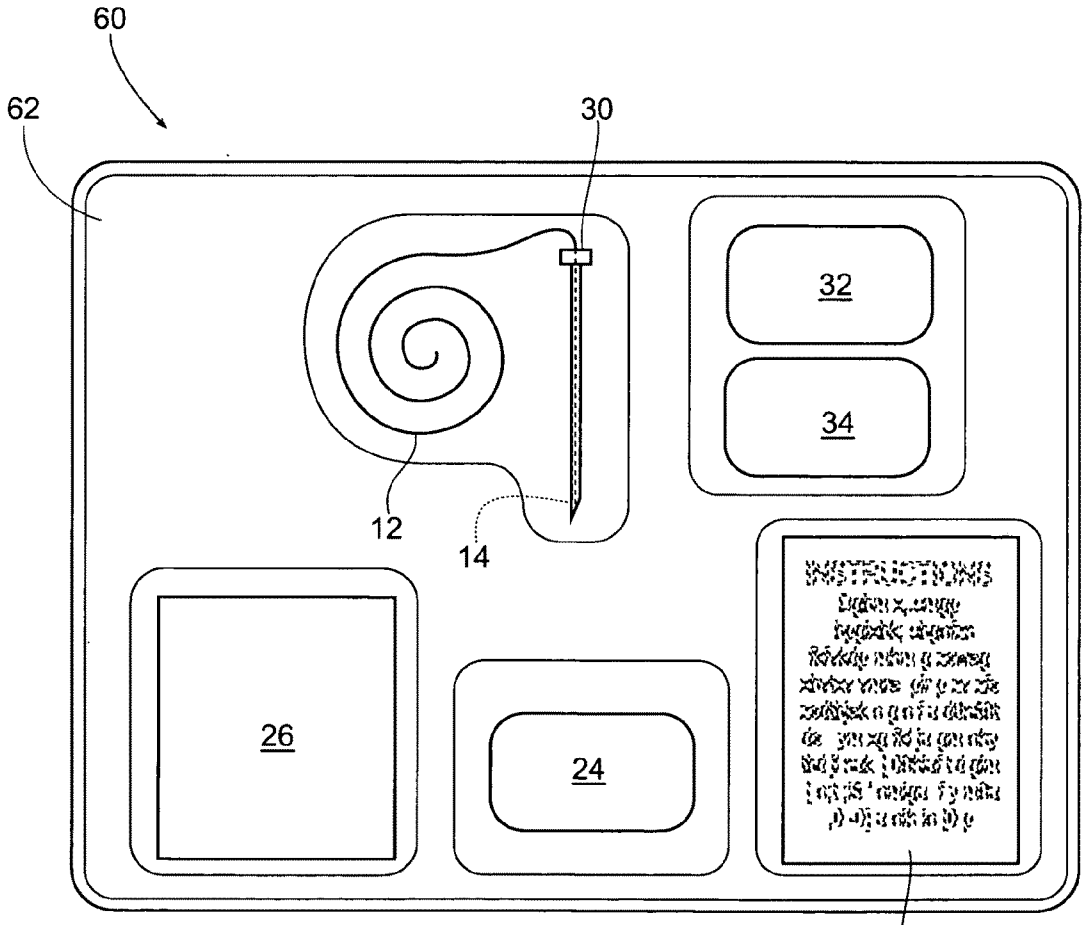


Fig. 12

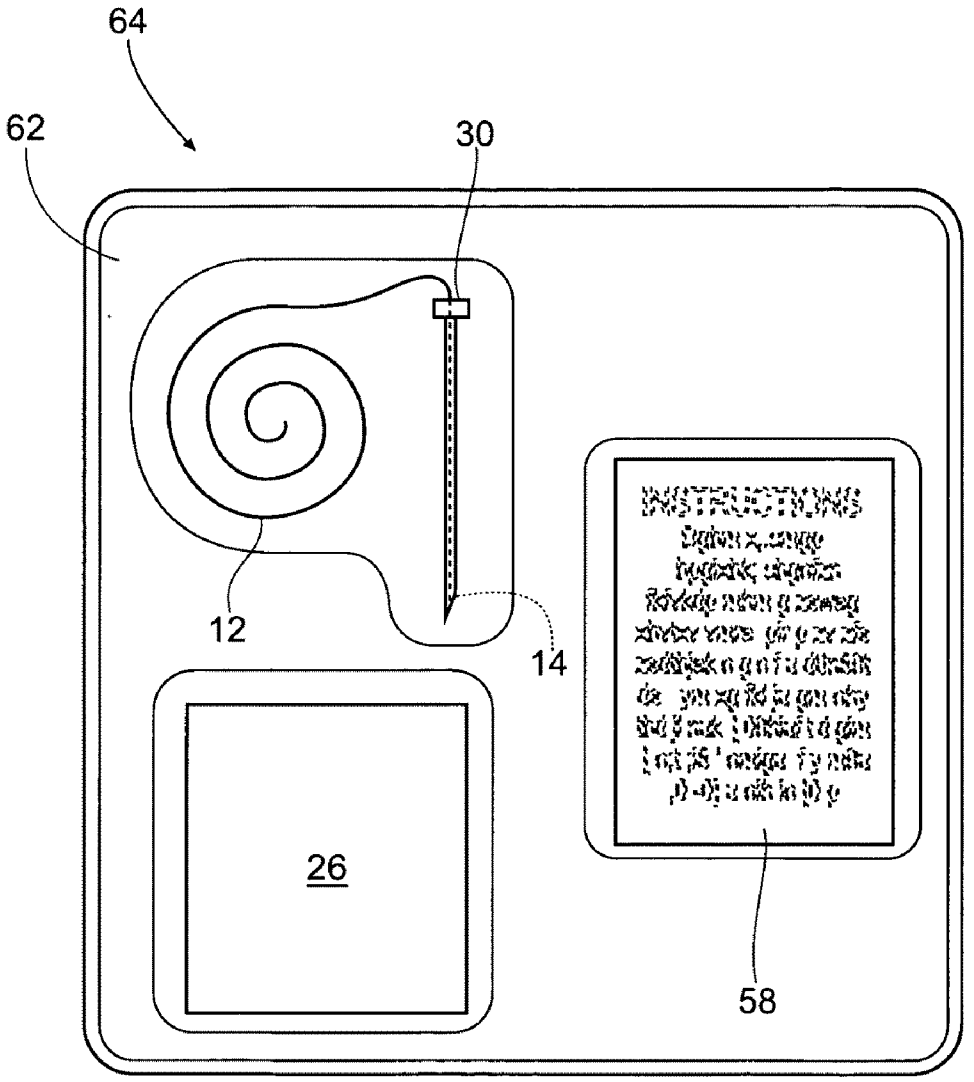


Fig. 13

SYSTEMS AND METHODS TO PLACE ONE OR MORE LEADS IN TISSUE FOR PROVIDING FUNCTIONAL AND/OR THERAPEUTIC STIMULATION

RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Patent Application Ser. No. 61/201,030, filed 5 Dec. 2008, and entitled "Systems and Methods to Place One or More Leads in Tissue for Providing Functional and/or Therapeutic Stimulation," which is incorporated herein by reference.

FIELD OF INVENTION

[0002] This invention relates to systems and methods for placing one or more electrode leads in tissue for providing electrical stimulation to tissue.

BACKGROUND OF THE INVENTION

[0003] Neurostimulation, i.e., neuromuscular stimulation (the electrical excitation of nerves and/or muscle to directly elicit the contraction of muscles) and neuromodulation stimulation (the electrical excitation of nerves, often afferent nerves, to indirectly affect the stability or performance of a physiological system) and brain stimulation (the stimulation of cerebral or other central nervous system tissue) can provide functional and/or therapeutic outcomes. While existing systems and methods can provide remarkable benefits to individuals requiring neurostimulation, many quality of life issues still remain. For example, existing systems include complicated procedures to place electrodes and pulse generators, and issues remain with the migration of electrodes which eventually reduce the effectiveness of the neurostimulation. Furthermore, these systems are, by today's standards, relatively large and awkward to manipulate, transport, and adhere to the patient.

[0004] There exist both external and implantable devices for providing neurostimulation in diverse therapeutic and functional restoration indications. These neuro-stimulators are able to provide treatment and/or therapy to individual portions of the body. The operation of these devices typically includes the use of an electrode placed either on the external surface of the skin and/or a surgically implanted electrode. In the case of external neurostimulators, surface electrode(s) and/or percutaneous lead(s) having one or more electrodes may be used to deliver electrical stimulation to the select portion of the patient's body.

[0005] One example of an indication where therapeutic treatment may be provided is for the treatment of pain, such as to provide a therapy to reduce pain in individuals with amputated limbs. Amputation leads to chronic pain in almost all (95%) patients, regardless of how much time had passed since the amputation (Ephraim et al. 2005). The pain can be extremely bothersome to amputees, significantly decrease their quality of life, correlate with increased risk of depression, and negatively affect their inter-personal relationships and their ability to return to work (Kashani et al 1983; Blazer et al. 1994; Cansever et al. 2003). The present methods of treatment, which are primarily medications, are unsatisfactory in reducing amputation-related pain, have unwanted side effects, offer a low success rate, and often lead to addiction.

[0006] Most amputees have two types of pain: residual limb (stump) pain and phantom pain. Approximately 72-85% of amputees have phantom pain and 68-76% of amputees have residual limb (stump) pain (Sherman and Sherman 1983; Sherman et al. 1984; Ehde et al. 2000; Ephraim et al. 2005). Both stump pain and phantom limb pain are chronic pains experienced after an amputation, and they are easily distinguished by the perceived location of the pain. Stump pain is sensed in the portion of the limb that remains after amputation, and phantom limb pain is perceived in the portion of the limb that has been removed. Typically, amputee patients with severe stump pain also have severe phantom limb pain, but it is recommended that their responses to treatment be measured independently (Jensen et al. 1985; Kooijman et al. 2000). Stump and phantom pain can be severe and debilitating to a large proportion of persons with amputations, who will unfortunately often progress through a battery of management techniques and procedures without finding relief from their pain (Bonica 1953; Sherman et al. 1980; Ehde et al. 2000; Loeser 2001a; Ephraim et al. 2005).

[0007] An estimated 80-95% of 1.7 millions persons who currently live with amputations plus the additional 185,000 persons expected to undergo amputation each year in the United States will suffer from stump and/or phantom pain at an annual direct cost of $1.4-2.7 billion and overall associated costs of $13 billion (Sherman and Sherman 1983; Sherman et al. 1984; Ehde et al. 2000; Mekhail et al. 2004; Ephraim et al. 2005). Severe post-amputation pain often leads to further disability, reduced quality of life, and frequently interferes with the simple activities of daily life more than the amputation itself (Millstein et al. 1985; Schoppen et al. 2001; Marshall et al. 2002; Whyte and Carroll 2002; Rudy et al. 2003), and no available therapy is sufficient to manage it (Sherman et al. 1980; Jahangiri et al. 1994; Rosenquist and Haider 2008).

[0008] Many techniques have been developed to treat post-amputation pain, but all of them are ultimately insufficient (Jahangiri et al. 1994). A review in 1980 found that none of the 68 treatments available for post-amputation pain were uniformly successful (Sherman et al. 1980), and more recent reviews have found that little has changed and there remains a large need for an effective method of treating stump and phantom pain (Davis 1993; Wall et al. 1994; Loeser 2001a; Halbert et al. 2002; Rosenquist and Haider 2008). Some studies report that as few as 1% of amputees with severe phantom and stump pain receive lasting benefit from any of the available treatments (Sherman and Sherman 1983; Sherman et al. 1984). Presently, most patients are managed with medications, but approximately a third of amputees still report severe (intensity of 7-10 on a scale of 0-10) phantom and stump pain.

[0009] Non-narcotic analgesics, such as acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDS), have relatively minor side effects and are commonly used for several types of pain. However, they are not specific to stump or phantom pain and are rarely sufficient in managing moderate to severe chronic post-amputation pain (Sherman et al. 1980; Loeser 2001a; Rosenquist and Haider 2008).

[0010] The use of narcotic analgesics, such as N-methyl-D-aspartate (NDMA) antagonists, has shown only minor success with inconsistent results. Narcotics carry the risk of addiction and side effects, such as nausea, confusion, vomiting, hallucinations, drowsiness, dizziness, headache, agitation, and insomnia. Several trials of multiple narcotic agents have failed to show statistically significant improvement in phantom pain (Stangl and Loeser 1997; Nikolajsen et al.

2000; Loeser 2001a; Maier et al. 2003; Hayes et al. 2004; Wiech et al. 2004; Rosenquist and Haider 2008).

[0011] Physical methods such as adjusting the prosthesis may be helpful, but only if the pain is due to poor prosthetic fit. Other physical treatments, including acupuncture, massage, and percussion or heating/cooling of the stump, have few complications but also have limited data to support their use and have not been well accepted clinically (Russell and Spalding 1950; Gillis 1964; Monga and Jaksic 1981; Loeser 2001a).

[0012] Psychological strategies, such as biofeedback and psychotherapy, may be used as an adjunct to other therapies but are seldom sufficient, and there are few studies demonstrating efficacy and these approaches are not specific to stump or phantom pain (Dougherty 1980; Sherman 1980). Mirror-box therapy has demonstrated mixed results and is not widely used in clinical practice (Ramachandran and Rogers-Ramachandran 1996; Brodie et al. 2007; Chan et al. 2007; Rosenquist and Haider 2008).

[0013] Many surgical procedures have been attempted, but few are successful and most are contraindicated for the majority of the amputee patients (Loeser 2001a). Because neuromas are implicated with stump and phantom pain, there have been many attempts to remove them surgically, but ultimately a new neuroma will develop each time a nerve is cut and the pain relief only lasts for the 3 weeks that it takes for a new neuroma to form (Sturm 1975; Sunderland 1978; Sherman 1980). Furthermore, neuroablative procedures carry the risk of producing deafferentation pain, and any surgical procedure has a greater chance of failure than success (Loser 2001a; Rosenquist and Haider 2008). Thus, present medical treatments of stump and phantom pain are inadequate, and most sufferers resort to living with pain that is poorly controlled with medications.

[0014] Electrical stimulation systems hold promise for relief of post-amputation pain, but widespread use of available systems is limited.

[0015] Transcutaneous electrical nerve stimulation (TENS) has been cleared by the FDA for treatment of pain and may be successful in reducing post-amputation pain. TENS systems are external neurostimulation devices that use electrodes placed on the skin surface to activate target nerves below the skin surface. TENS has a low rate of serious complications, but it also has a relatively low (i.e., less than 25%) long-term rate of success.

[0016] Application of transcutaneous electrical nerve stimulation (TENS) has been used to treat stump and phantom pain successfully, but it has low long-term patient compliance, because it may cause additional discomfort by generating cutaneous pain signals due to the electrical stimulation being applied through the skin, and the overall system is bulky, cumbersome, and not suited for long-term use (Nashold and Goldner 1975; Sherman 1980; Finsen et al. 1988).

[0017] Spinal cord stimulation (SCS) systems are FDA approved as implantable neurostimulation devices marketed in the United States for treatment of pain. Similar to TENS, when SCS evokes paresthesias that cover the region of pain, it confirms that the location of the electrode and the stimulus intensity should be sufficient to provide pain relief and pain relief can be excellent initially, but maintaining sufficient paresthesia coverage is often a problem as the lead migrates along the spinal canal (Krainick et al. 1980; Sharan et al. 2002; Buchser and Thomson 2003).

[0018] Lead migration is the most common complication for spinal cord stimulators occurring in up to 45-88% of the cases (North et al. 1991; Andersen 1997; Spincemaille et al. 2000; Sharan et al. 2002). When the lead migrates, the active contact moves farther from the target fibers and loses the ability to generate paresthesias in the target area. SCS systems attempt to address this problem by using leads with multiple contacts so that as the lead travels, the next contact in line can be selected to be the active contact.

[0019] Spinal cord stimulation is limited by the invasive procedure and the decrease in efficacy as the lead migrates. When it can produce paresthesias in the region of pain, spinal cord stimulation is typically successful initially in reducing stump and phantom pain, but over time the paresthesia coverage and pain reduction is often lost as the lead migrates away from its target (North et al. 1991; Andersen 1997; Loeser 2001a).

[0020] Brain stimulation systems are limited by the lack of patient selection criteria and the lack of studies demonstrating long-term efficacy.

[0021] Peripheral nerve stimulation may be effective in reducing post-amputation pain, but it previously required specialized surgeons to place cuff- or paddle-style leads around the nerves in a time consuming procedure.

[0022] Immediately following amputation, all patients experience short-term (postoperative) pain, but it usually resolves within a month as the wound heals. In contrast, a long-term pain often develops and persists in the stump and phantom limb after the amputated limb has healed into a healthy stump. Stump and phantom pain are thought to have a peripheral and central component, and both components may be mediated by stimulating the peripheral nerves that were transected during amputation.

[0023] Neuromas develop when a peripheral nerve is cut and the proximal portion produces new axon growth that forms a tangled mass as it fails to connect with the missing distal portion of the nerve. All amputations produce neuromas and not all neuromas are painful, but neuromas are thought to be a major source of pain after amputation (Burchiel and Russell 1987; Loeser 2001a; Rosenquist and Haider 2008). Neuromas may generate spontaneous activity (Wall and Gutnick 1974), and the level of activity in afferent fibers innervating the region of pain has been linked to the level of post-amputation pain (Nyström and Hagbarth 1981).

[0024] As previously described, electrical stimulation has been used and shown to be effective in treating amputee pain, but present methods of implementation have practical limitations that prevent widespread use. External systems are too cumbersome, and implanted spinal cord stimulation systems often have problems of lead migration along the spinal canal, resulting in either the need for frequent reprogramming or clinical failure.

[0025] It is time that systems and methods for providing neurostimulation address not only specific prosthetic or therapeutic objections, but also address the quality of life of the individual requiring neurostimulation, including a need to treat amputee pain with minimally-invasive systems and methods that may not require reprogramming, and include lead(s) that can be inserted percutaneously near target peripheral nerve(s) and resist(s) migration.

SUMMARY OF THE INVENTION

[0026] The invention provides improved systems and methods for placing one or more electrode leads in tissue for providing electrical stimulation to tissue to reduce pain.

[0027] One aspect of the invention provides lead placement procedures that may be used for placing a single electrode lead to activate a target nerve and/or nerves and/or nerve bundles (e.g., the brachial plexus, sciatic nerve, and/or femoral nerve, and/or their roots or branches) that carry the pain signal(s) in a system for the relief of neuropathic pain, such as post-amputation pain, but is not exclusive to this application. For example, if the pinky finger hurts, the systems and methods are well adapted to stimulate the ulnar nerve (which innervates the pinky finger). The procedures optimally allow using only a single lead, although it is to be appreciated that more than one lead(s) may be used, to activate a greater range of target nerves and/or nerve bundles.

[0028] Other features and advantages of the inventions are set forth in the following specification and attached drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0029] FIG. **1** is an anatomical view of a patient utilizing one embodiment of the present invention, including a percutaneous electrode lead coupled to an external pulse generator.

[0030] FIG. **2** is an anatomical view of a patient utilizing another embodiment of the present invention, including an implanted electrode lead coupled to an implanted pulse generator.

[0031] FIGS. **3**A and **3**B are anatomical views of a patient's shoulder showing the anatomical landmarks useful to guide the placement of a needle electrode as a component and/or step of the present invention.

[0032] FIG. **4** is an anatomical view of the shoulder as shown in FIG. **3**B, showing infraclavicular and subcoracoid neuroanatomy with a needle introducer depicting a direction of lead insertion toward the brachial plexus.

[0033] FIG. **5** is an anatomical view similar to FIG. **4**, except showing greater detail of the brachial plexus and the lead insertion, and showing an anticipated region of activation.

[0034] FIG. **6** is an anatomical cross-sectional view (perpendicular to the axis of the lead insertion) of the brachial plexus and surrounding tissue.

[0035] FIG. **7** is an anatomical view of the shoulder as shown in FIG. **3**B, showing the percutaneous lead inserted through the skin in the target area in the shoulder via an introducer needle.

[0036] FIG. **8** is an anatomical view of the shoulder as shown in FIG. **7**, showing the percutaneous lead coupled to the external pulse generator and the return electrode.

[0037] FIG. **9** is a view of a possible electrode lead for use with the systems and methods of the present invention.

[0038] FIGS. **10** and **11** are perspective views of another possible electrode lead for use with the systems and methods of the present invention, the lead including anchoring members.

[0039] FIG. **12** is a plan view of a kit packaging the systems and methods components for use, along with instructions for use.

[0040] FIG. **13** is a plan view of an additional kit packaging the systems and methods components for use, along with instructions for use.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0041] Although the disclosure hereof is detailed and exact to enable those skilled in the art to practice the invention, the physical embodiments herein disclosed merely exemplify the invention which may be embodied in other specific structures. While the desired embodiment has been described, the details may be changed without departing from the invention.

[0042] The various aspects of the invention will be described in connection with the placement of one or more leads **12** having one or more electrodes **14**, in tissue, e.g., on, in, or near nerves and/or muscles, for improved recruitment of targeted nerves or muscles for prosthetic or therapeutic purposes, such as for the treatment of post-amputation pain. That is because the features and advantages that arise due to the invention are well suited to this purpose. Still, it should be appreciated that the various aspects of the invention can be applied to achieve other objectives as well.

I. Reduction of Post-Amputation Pain

[0043] The present novel invention provides systems and methods for the reduction of pain. Most amputees have two types of pain: residual limb (stump) pain and phantom pain. The systems and methods of the present invention are adapted to reduce either and/or both types of pain by stimulating target nerves, generally on the same side of the body as the amputation, i.e., the nerves that innervate the regions of pain. It is to be appreciated that amputation can include any or all portions of a limb, including arms and legs in both humans and animals.

[0044] The present novel invention provides systems and methods that place percutaneous electrode lead(s) **12** appropriately in patients with amputations to electrically activate a target nerve and/or nerves and/or nerve bundles (e.g., the brachial plexus, sciatic nerve, and/or femoral nerve, and/or their roots or branches) that carry the pain signal(s). For example, if the pinky finger hurts, the systems and methods are well adapted to stimulate the ulnar nerve (which innervates the pinky finger). If electrical stimulation activates the target nerve sufficiently at the correct intensity, then the patient will feel a comfortable tingling sensation called a paresthesia in the same region as their pain. It is to be appreciated that the sensation could be described with other words such as buzzing, thumping, etc. Just as the patient can have pain in the stump and/or the phantom limb, electrical stimulation can evoke paresthesias that the patient also feels in the stump and/or phantom limb. Evoking paresthesias in the regions of pain confirms correct lead placement and indicates stimulus intensity is sufficient to reduce pain.

[0045] The ability to insert the lead **12** percutaneously near a target peripheral nerve simplifies the approach to a quick (e.g., 5, or 10, or 20 minute) procedure, such as an out-patient procedure that can be performed in a standard community-based clinic, allowing widespread use and providing a minimally-invasive screening test to determine if patients will benefit from the systems and methods of the present invention, including a percutaneous system **10** and/or a fully implanted system **11** (see FIGS. **1** and **2**).

[0046] The systems and methods of the present invention are well suited to place a percutaneous lead **12** on, in, or near the brachial plexus with a quick procedure to generate electrically a comfortable (tingling) sensation of paresthesia in the regions of stump and phantom pain and reduce the patients' pain.

[0047] In a percutaneous system **10**, the lead **12** may be percutaneously placed near the brachial plexus and exit at the skin puncture site **16** and coupled to an external pulse generator **26**. The percutaneously placed lead **12** and external

pulse generator **26** may provide a screening test function to confirm paresthesia coverage and/or pain relief of the painful areas. If the screening test is successful, the patient may proceed to a home-trial (e.g., a day, week, month, year) to determine if pain relief can be sustained in the home environment. If either the screening test or home trial is unsuccessful, the lead **12** may be quickly and easily removed. It is to be appreciated that a home-trial is not a requirement for either the percutaneous system or a fully implanted system.

[0048] However, if the screening test and/or home-trial are successful, the patient's percutaneous system may be converted into a fully implanted system **11** by replacing the external pulse generator **26** with an implantable pulse generator **28** that is implanted in a convenient area (e.g., the subclavicular area), and coupling a new sterile lead **12**, or a sterile lead extension, to the implantable pule generator **28**.

[0049] Inserting the lead **12** percutaneously allows the lead **12** to be placed quickly and easily, and placing the lead **12** in a peripheral location, where it is less likely to be dislodged, addresses the lead migration problems of spinal cord stimulation that result in decreased paresthesia coverage, decreased pain relief, and the need for frequent patient visits for reprogramming.

[0050] In the exemplary embodiment of the present invention, placing the percutaneous lead **12** in adipose tissue of the infraclavicular and subcoracoid space near the brachial plexus (to be described in greater detail below), may minimize complications related to lead movement. Perineural catheters connected to infusion pumps have been placed in similar locations for use by ambulatory patients in their home environment and have a low rate of catheter dislocations and complications (Wilson et al 1998; Ekatodramis and Borgeat 2000; Ilfeld et al. 2002).

[0051] In the percutaneous system **10**, an electrode lead **12**, such as a coiled fine wire electrode lead may be used because it is minimally-invasive and previous studies suggest it will perform well in this location and tissue type during use.

[0052] In the fully implanted system **11**, the same or different electrode lead **12** may be used, such as a slightly larger electrode lead that may be sized and configured to withstand greater mechanical forces and resist migration during long-term use. A larger electrode lead **12** may be sized and configured to withstand forces in excess of those anticipated near the brachial plexus, and other similarly flexible regions of the body.

II. Implanting the Electrode Lead

[0053] A. The Anatomic Landmarks

[0054] As already described, certain components of the systems and methods of the present invention are well adapted to be implanted in a particular location near the patient's shoulder, where it has been discovered that effective stimulation of the nerves of the brachial plexus can be achieved with a single electrode lead **12** to reduce pain. As can be seen in FIGS. **3**A and **3**B, the main anatomic landmarks guiding the unique placement of these components are the clavicle and the coracoid process.

[0055] FIG. **4** shows the clavicle as a doubly curved short bone that connects the arm (upper limb) to the body (trunk), located directly above the first rib. It acts as a shunt to keep the scapula in position so the arm can hang freely. The coracoid process is a small finger-like structure on the upper lateral corner of the scapula. Pointing laterally forward, it, together with the acromion, serves to stabilize the shoulder joint. It is palpable in the deltopectoral groove between the deltoid and pectoralis major muscles.

[0056] Guided by these landmarks, the brachial plexus can be identified. Referring to FIGS. **4** and **5**, the brachial plexus comprises an arrangement of nerve fibers, running from the spine, formed by the ventral rami of the lower cervical and upper thoracic nerve roots, specifically from above the fifth cervical vertebra to underneath the first thoracic vertebra (C5-T1). It proceeds through the neck, under the clavicle and generally anterior to the scapula, through the armpit region and into the arm. The brachial plexus is generally responsible for cutaneous and muscular innervation of the entire upper limb, with only two exceptions; the trapezius muscle is innervated by the spinal accessory nerve and an area of skin near the armpit is innervated by the intercostobrachialis nerve.

[0057] FIG. **6** is a cross-sectional view (perpendicular to the axis of the lead insertion) of the brachial plexus and surrounding tissue (Moayeri et al. 2008). As can be seen in FIG. **6**, the brachial plexus is surrounded by a large amount of adipose tissue **54** in the infraclavicular and subcoracoid regions, where the electrode lead **12** will be placed, and is well suited for use in adipose tissue. In the infraclavicular and subcoracoid sections of cadavers studied, the brachial plexus was surrounded by about 6.90 ± 1.82 cm^2 to about 7.06 ± 1.48 cm^2, which is ample area to place the electrode lead **12**.

[0058] B. Implantation Methodology

[0059] Representative lead insertion techniques will now be described to place an electrode lead **12** in a desired location in adipose tissue **54** at or near the brachial plexus. It is this desired placement that makes possible the stimulation of the brachial plexus with a single lead **12** to provide pain relief.

[0060] FIGS. **7** and **8** show representative embodiments of the steps that representative instructions for use **58** can incorporate or direct for the placement of an electrode lead **12** in a targeted tissue region for the relief of pain, such as post-amputation pain. The instructions may include a series of steps that can be followed to carry out portion or portions of the procedure. These steps may include, but are not limited to:

[0061] 1) Place the patient in a supine position with head turned away from the lead insertion site **16** and forearm laid to rest in a neutral position beside the body.

[0062] 2) Prepare the lead insertion site with antiseptic and local subcutaneous anesthetic (e.g., 2% lidocaine).

[0063] 3) Locate the site of skin puncture **16** with landmarks as necessary, such as those previously described, e.g., approximately 2 cm medial and caudal to the coracoid process.

[0064] 4) Insert a sterile percutaneous electrode lead **12** at a predetermined angle based on landmarks used, e.g., approximately 45 degrees towards the top of the axillary fossa in relation to the axillary artery. The lead **12** may be preloaded in the introducer needle **30** (see FIG. **7**).

[0065] 5) Place a surface stimulation return electrode **24** in proximity of the area in which the percutaneous lead **12** has been placed. Test stimulation will be applied to the lead **12**, with the surface electrode **24** providing a return path. The surface electrode **24** may be placed adjacent to the lead. Its position is not critical to the therapy and it can be moved throughout the therapy to reduce the risk of skin irritation.

[0066] 6) Couple the lead **12** to the external pulse generator **26** and to the return electrode **24** (see FIG. **8**). Set the desired stimulation parameters. Test stimulation may be delivered using a current-regulated pulse generator, for example. The

external pulse generator **26** may be programmed to 4 mA, 100 μs, 100 Hz, and an on-off duty cycle of 0.25 sec., as a non-limiting example.

[0067] 7) Advance the introducer slowly until the subject reports the first evoked sensation in the stump or phantom upper limb (e.g., hand). Progressively reduce the stimulus amplitude and advance the introducer more slowly until the sensation can be evoked in the phantom upper limb at a predetermined stimulus amplitude (e.g., 1 mA). Stop the advancement of the introducer, and increase the stimulus amplitude in small increments (e.g., 0.1 mA) until the stimulation-evoked tingling sensation (paresthesia) expands to overlay the entire region of pain in the subject's stump and phantom limb.

[0068] It is expected to locate the brachial plexus after inserting the introducer approximately 4 cm from the site of skin puncture **16**. At this depth, it is expected that a low stimulus intensity may evoke comfortable sensations (paresthesia) without generating muscle contraction (Nashold and Goldner 1975; Picaza et al. 1975; Nashold et al. 1982).

[0069] 8) Withdraw the introducer **30**, leaving the percutaneous lead **12** in proximity to the brachial plexus.

[0070] 9) Cover the percutaneous exit site and lead **12** with a bandage **32**. A bandage **34** may also be used to secure the external portion of the lead **12** (or an extension cable used to couple the lead **12** to the external pulse generator) to the skin (see FIG. **1**). It is expected the length of time to place the lead **12** to be less than 10 minutes, although the process may be shorter or longer.

[0071] 10) Vary the stimulus amplitude in small steps (e.g., 0.1-0.5 mA) to determine the thresholds at which stimulation evokes first sensation (T_{SEN}), sensation (paresthesia) superimposed on the region of pain (T_{SUP}), muscle twitch (T_{MUS}) of the triceps brachii (innervated by the radial nerve branch of the brachial plexus), and maximum comfortable sensation (T_{MAX}). Query the subject at each stimulus amplitude to determine sensation level, and visually monitor muscle response. Record the results.

[0072] 11) It is possible that stimulation intensity may need to be increased slightly during the process due to causes such as habituation or the subject becoming accustomed to sensation, but the need for increased intensity is unlikely and usually only occurs after several days to weeks to months as the tissue encapsulates and the subject accommodates to stimulation (Nashold 1975; Krainick and Thoden 1981; Goldman et al. 2008). It is to be appreciated that the need for increased intensity could happen at any time, even years out, which would likely be due to either lead migration or habituation, but may also be due reasons ranging from nerve damage to plasticity/reorganization in the central nervous system.

[0073] 12) If paresthesias cannot be evoked with the initial lead placement, redirect the introducer **30** either caudal or cephalad, but avoid the lung by never directing the needle introducer **30** medially.

[0074] 13) If sensations still cannot be evoked in a given subject, then the muscle twitch response of the triceps brachii may be used to guide lead placement and then increase stimulus intensity until sufficient paresthesias are elicited in the stump and phantom limb. Minimal muscle contraction may be acceptable if it is well tolerated by the amputee patient in exchange for significant pain relief and if it does not lead to additional discomfort or fatigue (Long 1973).

[0075] 14) If stimulation evokes muscle contraction at a lower stimulus threshold than paresthesia (e.g. if $T_{MUS} \leqq T_{SUP}$) and contraction leads to discomfort, then a lower stimulus frequency (e.g., 12 Hz) may be used because low frequencies (e.g., 4-20 Hz) have been shown to minimize discomfort due to muscle contraction and provide >50% relief of shoulder pain in stroke patients while still inhibiting transmission of pain signals in the central nervous system in animals (Chung et al. 1984; Yu et al. 2001, 2004; Chae et al. 2005). If continued muscle contraction leads to pain due to fatigue, change the duty cycle, using parameters shown to reduce muscle fatigue and related discomfort in the upper extremity (e.g. 5 s ramp up, 10 s on, 5 s ramp down, 10 s off) (Yu et al. 2004; Chae et al. 2005).

[0076] 15) If stimulation fails to elicit paresthesia in all areas of pain, then a second percutaneous lead **12'** (not shown) may need to be placed to stimulate the nerves that are not activated by the first lead **12**. If paresthesia coverage is incomplete, it may likely be due to insufficient activation of the musculocutaneous nerve because it has the most proximal branch point relative to the other nerves and is the most likely to be missed during single-injection nerve blocks of the brachial plexus. To place a lead near the musculocutaneous nerve, use the modified coracoid approach (a double-stimulation technique) that targets the musculocutaneous nerve in addition to the main trunk of the brachial plexus, as described above (Desroches 2003; Minville et al. 2005).

[0077] 16) If stimulation is successful, i.e., if the screening test and/or home-trial are successful, the patient's percutaneous system **10** (see FIG. **1**) may be converted into a fully implanted system **11** by replacing the external pulse generator **26** with an implantable pulse generator **28** that is implanted in a convenient area (e.g., the subclavicular area). In one embodiment, the electrode lead **12** used in the screening test and/or home-trial may be totally removed and discarded, and a new completely implantable lead may be tunneled subcutaneously and coupled to the implantable pulse generator. In an alternative embodiment, a two part lead may be incorporated in the screening test and/or home-trial where the implantable part is completely under the skin and connected to a percutaneous connector (i.e., extension) that can be discarded after removal. The implantable part may then be tunneled and coupled to the implantable pulse generator, or a new sterile extension may be used to couple the lead to the implantable pulse generator.

III. Electrode Lead Configurations

[0078] It is to be appreciated that the configuration of one or more leads **12** and electrodes **14**, and the manner in which they are implanted can vary. Stimulation may be applied through an electrode lead **12**, such as a fine wire electrode, paddle electrode, intramuscular electrode, or general-purpose electrode, inserted via a needle introducer or surgically implanted in proximity of the target site. Once proper placement is confirmed, the needle may be withdrawn, leaving the electrode in place. Stimulation may also be applied through a penetrating electrode, such as an electrode array comprised of any number (i.e., one or more) of needle-like electrodes that are inserted into the target site. In both cases, the lead may placed using a needle-like introducer, allowing the lead/electrode placement to be minimally invasive.

[0079] The electrode **14** may be electrically insulated everywhere except at one (monopolar), or two (bipolar), or three (tripolar), for example, conduction locations near its distal tip. Each of the conduction locations may be connected to one or more conductors that run the length of the electrode

and lead **12**, proving electrical continuity from the conduction location through the lead **12** to the stimulator **26** or **28**.

[0080] The electrode lead **12** is desirably provided in a sterile package, and may be pre-loaded in the introducer needle **30**. The lead **12** desirably possess mechanical properties in terms of flexibility and fatigue life that provide an operating life free of mechanical and/or electrical failure, taking into account the dynamics of the surrounding tissue (i.e., stretching, bending, pushing, pulling, crushing, etc.). The material of the electrode desirably discourages the in-growth of connective tissue along its length, so as not to inhibit its withdrawal at the end of its use. However, it may be desirable to encourage the in-growth of connective tissue at the distal tip of the electrode, to enhance its anchoring in tissue.

[0081] One embodiment of the lead **12** shown in FIG. **9** may comprise a minimally invasive coiled fine wire lead **12** and electrode **14**. The electrode **14** may also include, at its distal tip, an anchoring element **48**. In the illustrated embodiment, the anchoring element **48** takes the form of a simple barb or bend. The anchoring element **48** is sized and configured so that, when in contact with tissue, it takes purchase in tissue, to resist dislodgement or migration of the electrode out of the correct location in the surrounding tissue. Desirably, the anchoring element **48** is prevented from fully engaging body tissue until after the electrode **14** has been deployed. The electrode may not be deployed until after it has been correctly located during the implantation (lead placement) process, as previously described.

[0082] An alternative embodiment of an electrode lead **12** shown in FIGS. **10** and **11**, may also include, at or near its distal tip or region, one or more anchoring element(s) **70**. In the illustrated embodiment, the anchoring element **70** takes the form of an array of shovel-like paddles or scallops **76** proximal to the proximal-most electrode **14** (although a paddle **76** or paddles could also be proximal to the distal most electrode **14**, or could also be distal to the distal most electrode **14**). The paddles **76** as shown are sized and configured so they will not cut or score the surrounding tissue. The anchoring element **70** is sized and configured so that, when in contact with tissue, it takes purchase in tissue, to resist dislodgement or migration of the electrode out of the correct location in the surrounding tissue (e.g., soft adipose tissue **54**). Desirably, the anchoring element **70** is prevented from fully engaging body tissue until after the electrode **14** has been deployed. The electrode is not deployed until after it has been correctly located during the implantation (lead placement) process, as previously described. In addition, the lead **12** may include one or more ink markings **74**, **75** to aid the physician in its proper placement.

[0083] Alternatively, or in combination, stimulation may be applied through any type of nerve cuff (spiral, helical, cylindrical, book, flat interface nerve electrode (FINE), slowly closing FINE, etc.) that is surgically placed within muscle at the target site.

[0084] In all cases, the lead may exit through the skin and connect with one or more external stimulators **26**, or the lead(s) may be routed subcutaneously to one or more implanted pulse generators **28**, or they may be connected as needed to internal and external coils for RF (Radio Frequency) wireless telemetry communications or an inductively coupled telemetry to control the implanted pulse generator. The implanted pulse generator **28** may be located some distance (remote) from the electrode **14**, or an implanted pulse generator may be integrated with an electrode(s), eliminating the need to route the lead subcutaneously to the implanted pulse generator.

[0085] Control of the stimulator and stimulation parameters may be provided by one or more external controllers. In the case of an external stimulator, the controller may be integrated with the external stimulator. The implanted pulse generator external controller (i.e., clinical programmer) may be a remote unit that uses RF (Radio Frequency) wireless telemetry communications (rather than an inductively coupled telemetry) to control the implanted pulse generator. The external or implantable pulse generator may use passive charge recovery to generate the stimulation waveform, regulated voltage (e.g., 10 mV to 20 V), and/or regulated current (e.g., about 10 μA to about 50 mA). Passive charge recovery is one method of generating a biphasic, charge-balanced pulse as desired for tissue stimulation without severe side effects due to a DC component of the current.

[0086] The neurostimulation pulse may by monophasic, biphasic, and/or multi-phasic. In the case of the biphasic or multi-phasic pulse, the pulse may be symmetrical or asymmetrical. Its shape may be rectangular or exponential or a combination of rectangular and exponential waveforms. The pulse width of each phase may range between e.g., about 0.1 μsec. to about 1.0 sec., as non-limiting examples.

[0087] Pulses may be applied in continuous or intermittent trains (i.e., the stimulus frequency changes as a function of time). In the case of intermittent pulses, the on/off duty cycle of pulses may be symmetrical or asymmetrical, and the duty cycle may be regular and repeatable from one intermittent burst to the next or the duty cycle of each set of bursts may vary in a random (or pseudo random) fashion. Varying the stimulus frequency and/or duty cycle may assist in warding off habituation because of the stimulus modulation.

[0088] The stimulating frequency may range from e.g., about 1 Hz to about 300 Hz, and the frequency of stimulation may be constant or varying. In the case of applying stimulation with varying frequencies, the frequencies may vary in a consistent and repeatable pattern or in a random (or pseudo random) fashion or a combination of repeatable and random patterns.

IV. System Kits

[0089] As FIGS. **12** and **13** show, the various devices and components just described can be consolidated for use in one or more functional kit(s) **60**, **64**. The kits can take various forms and the arrangement and contents of the kits can vary. In the illustrated embodiments, each kit **60**, **64** comprise a sterile, wrapped assembly. Each kit **60**, **64** includes an interior tray **62** made, e.g., from die cut cardboard, plastic sheet, or thermo-formed plastic material, which hold the contents. Kits **60**, **64** also desirably includes instructions for use **58** for using the contents of the kit to carry out the procedures described above, including the systems and methods incorporating the percutaneous system **10** and/or the implanted system **11**.

[0090] The instructions **58** can, of course vary. The instructions **58** may be physically present in the kits, but can also be supplied separately. The instructions **58** can be embodied in separate instruction manuals, or in video or audio tapes, CD's, and DVD's. The instructions **58** for use can also be available through an internet web page.

[0091] The foregoing is considered as illustrative only of the principles of the invention. Furthermore, since numerous modifications and changes will readily occur to those skilled

in the art, it is not desired to limit the invention to the exact construction and operation shown and described. While the desired embodiment has been described, the details may be changed without departing from the invention.

[0092] Various features of the invention are set forth in the following Claims.

We claim:

1. A method comprising:

placing an electrode at a targeted tissue region,

providing neurostimulation to the electrode at the targeted tissue region,

activating the targeted tissue region via the neurostimulation, and

causing the reduction of post-amputation pain.

2. The method according to claim **1**:

wherein the targeted tissue region further comprises a brachial plexus.

3. The method according to claim **2**:

wherein the targeted tissue region further comprises a region of adipose tissue on, in, or near the brachial plexus.

4. A system comprising:

a single lead having at least one electrode placed on, in, or near a brachial plexus, and

a stimulator adapted to provide neurostimulation to the lead and to stimulate the brachial plexus to reduce pain.

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