NUVECTRA™

Algovita® Spinal Cord Stimulation System
Information for Prescribers

℞ ONLY

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Indications for Use

The Algovita® Spinal Cord Stimulation (SCS) System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain, and leg pain.

Contraindications

Diathermy. Shortwave, microwave and/or therapeutic ultrasound diathermy must not be used on SCS patients. The energy generated by diathermy can be transferred through the SCS system, causing tissue damage at the lead site which may result in severe injury or death.

Failed Stimulation Trial. Patients who have failed to receive effective pain relief during a stimulation trial.

Implant Considerations for MR Conditional Scans

Under certain conditions, some fully implanted Algovita SCS Systems are magnetic resonance (MR) Conditional. Algovita Trial Stimulation Systems are not MR Conditional.

Algovita Trial Stimulation System

Warning: Patients with an Algovita Trial Stimulation System must not be exposed to MRI scans. The electronic magnetic field generated by an MRI scan may forcefully dislodge the leads, damage the trial stimulator electronics, and induce voltage through the leads that may cause an uncomfortable or jolting sensation or serious injury. The Algovita Trial Stimulation System components have not been tested for heating or migration in the MR environment. Introducing a patient with an Algovita Trial Stimulation System into an MRI scanner may result in severe patient injury or component malfunction.

Algovita SCS System

An Algovita SCS System is MR Conditional for an MRI examination of the head only if all components are listed as MR Conditional in *Table 1*, the components are fully implanted in approved locations, and all other Algovita SCS System, patient, and MRI system conditions are met. See the Algovita SCS System MRI Procedure Guidelines for complete warnings, precautions, and instructions for MR conditions of use.

Warnings:

- Algovita SCS System components are MR Conditional only when implanted in approved locations:
  - » Stimulator—Buttocks, abdomen (T1 or lower), or flank
  - » Leads—Epidural space
  - » Extensions—Connected to the lead and stimulator
  - » Anchors—Placed on the lead
  - » Port plugs—Inserted in the stimulator connector port

  See the Algovita SCS System MRI Procedure Guidelines for complete information.
- Algovita SCS System leads, stimulators, anchors, and port plugs implanted in other locations are untested for an MR environment.
- Do not take the Clinician Programmer, Programmer Charger, Pocket Programmer, or programmer accessories (for example, a charging paddle or power cord) into an MR environment, such as an MR scanner room. Algovita SCS System programmers and programmer accessories are MR Unsafe.

Table 1. Algovita SCS System Component MR Status

Algovita SCS System Component	MR Conditional	Components NOT evaluated for use in an MR environment
Stimulator	2408, 2412	
8 or 12-electrode percutaneous lead	1081-45, 1081-60, 1081-75 1084-45, 1084-60, 1084-75 1121-45, 1121-60, 1021-75 1124-45, 1124-60, 1124-75	1081-90, 1084-90, 1121-90, 1124-90 1086-45, 1086-60, 1086-75, 1086-90 1126-45, 1126-50, 1126-75, 1126-90
Paddle lead	3000-45, 3000-60 3101-45, 3101-60	
Extension	5208-40, 5212-40	5208-20, 5208-60, 5212-20, 5212-60
Anchor	5400	
Port plug	5510	

Warnings

Electrocautery. Electrocautery devices should not be used in close proximity to an implanted SCS system. Contact between an active electrode and an implanted SCS system component can cause direct stimulation of the spinal cord, which may result in severe injury to the patient.

If electrocautery is necessary, follow these precautions:

- Before using electrocautery, turn off the implantable pulse generator (IPG).
- If a lead or extension is attached to a external pulse generator (EPG), disconnect the EPG prior to using electrocautery.
- Use only bipolar cautery.
- After using electrocautery, confirm that the IPG is functioning as intended.

Electromagnetic Interference (EMI). EMI is a field of energy generated by equipment found in the home, work, medical, or public environments that is strong enough to interfere with IPG function. The Algovita SCS System is designed to be immune from common sources of electromagnetic interference.

Strong EMI can result in:

- **Serious injury,** resulting from heating of the implanted components that causes damage to surrounding tissue
- **System damage,** resulting in loss or change in symptom control requiring surgical replacement
- **Operational changes to the IPG,** causing stimulation to turn on or off, resetting to default clinician settings, or losing stimulation which can result in a return of symptoms
- **Unexpected changes in stimulation,** causing a momentary increase in stimulation which may cause an uncomfortable or jolting sensation

If any system components (IPG, leads, lead fragments, or extensions) remain implanted in the patient after a partial system explant, the patient is still susceptible to the above listed adverse effects.

The most common sources of EMI are discussed below.

- **Hospital or Medical Environments**

  Patients should always inform healthcare personnel that they have an implanted Algovita SCS System (and show their patient identification card) before any procedure is performed. Many diagnostic procedures, such as x-rays and ultrasounds, may be performed without

affecting the Algovita SCS System. However other diagnostic and therapeutic equipment with higher energy levels may interfere with the Algovita SCS System. Refer to the individual contraindications, warnings, and precautions for specific information.

- **Home, Work, or Public Environments**

  The patient should avoid or exercise caution when in the presence of the following potential sources of EMI that may affect the operation of the IPG:

  - Radiofrequency identification (RFID) sources
  - **Theft detectors or security screeners such as those used at entrances or exits of department stores, libraries, and other public establishments, and airport security screening devices.** Patients should exercise caution when approaching such a device and should request assistance to bypass the device. If the patient must proceed through the device, the patient should turn the IPG off and proceed with caution, moving through the center of the screener as quickly as possible.
  - Power lines and transmission towers
  - Electric substations, power generators, and large transformers
  - Portable and mobile RF communications equipment
  - Electric arc welding equipment
  - Electric steel furnaces
  - Electric induction heaters
  - Electric fences
  - Body fat measurement scales
  - Jackhammers
  - Stun guns

  The following commonly used items should not affect the operation of the IPG:

  - Cell phones and Bluetooth devices
  - Electric toothbrushes, electric shavers, and hair trimmers
  - Microwave ovens
  - Appliances such as washing machines, dryers, electric stoves, toasters, blenders, electric can openers, and food processors
  - Electric blankets and heating pads

- » Personal computers, electric typewriters, copiers, and fax machines
- » Televisions, AM/FM radios, stereos, and personal music players
- » Vacuum cleaners and electric brooms

For additional information about devices that generate electromagnetic interference contact Nuvectra™. If a patient suspects EMI is disrupting the operation of their SCS system, advise the patient to move away from the source of the EMI.

Heat Due to Charging. Advise patients not to charge the IPG while they are sleeping. While charging, the charging paddle may become too warm, which could result in a burn. Failure to use the adjustable belt or an adhesive patch as shown in the charging instructions may also result in a burn.

IPG Case Damage. Burns may result if the IPG case is ruptured or pierced, exposing patient tissue to battery chemicals.

Other Active Implanted Medical Devices. Algovita SCS System interactions with other active implantable medical devices (such as pacemakers, defibrillators, implanted spinal cord and peripheral nerve stimulators, deep brain stimulators, implantable infusion pumps, cochlear implants, and vagus nerve stimulators) are not known. Exercise caution when other implanted devices are operating concurrently with the Algovita SCS System. Possible effects include sensing problems and inappropriate device responses.

Magnet. If a magnet is prescribed, do not use the magnet near implanted medical devices such as pacemakers, cardioverter defibrillators (ICDs), or other neurostimulation systems. The magnet may interfere with the operation of these implanted devices, which may change the therapy delivered by the device.

Modification. Do not modify the Clinician Programmer, Patient Feedback Tool, EPG, Programmer Charger, Pocket Programmer, or charging accessories. Modification of any SCS system component may result in damage to the system, compromised system integrity, and harm or injury to the patient.

Programmer Interaction with Other Implanted Devices. Do not charge the IPG, use the Patient Feedback Tool, or use the Clinician Programmer, Programmer Charger, or Pocket Programmer to change program settings when near a person who has a pacemaker, defibrillator, SCS system, or other implanted device. The effects of the Patient Feedback Tool or Algovita programmers on other implanted devices are unknown.

Radio-frequency or Microwave Ablation. Safety has not been established for radiofrequency (RF) or microwave ablation in patients who have an SCS system. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.

Precautions

Physician Training. Physicians should be experienced in the diagnosis and treatment of chronic pain syndromes and have undergone surgical and/or device implantation training.

Allergic Reaction to Product Materials. SCS systems have materials that come in contact or may come in contact with tissue. Before the system is implanted, determine whether a patient may have an allergic reaction to implanted component materials, external component materials including the charging paddle and optional adhesive patches.

Incompatibility of Algovita Clinician Programmer with Other Medical Devices. The effects of using the Algovita Clinician Programmer to interrogate other electronic, programmable devices such as pacemakers, defibrillators, cochlear implants, other neurostimulators, or CPAP machines are unknown. One effect could be the reprogramming of the other device. Physicians familiar with each device should check the programmed parameters of each device before the patient is discharged and after each programming session of either device.

IPG Location. When determining the IPG pocket location, do not create a pocket close to bony structures or areas of pressure or restriction. Creating a pocket in these areas may cause patient discomfort or lead migration.

Patients Who Are Poor Surgical Risks. Do not implant an SCS system if a patient is considered a poor surgical risk. Implanting an SCS system has risks similar to surgical procedures of the spine, including spinal fluid leak, headaches, swelling, bruising, bleeding, infection, or paralysis.

Use in Pediatric, Pregnant, or Nursing Patients. Safety and effectiveness of SCS has not been established for pediatric patients, for use during pregnancy, or for use with nursing patients.

Preoperative Considerations

Antibiotics. To help prevent infection, use prophylactic antibiotics. An infection may require the removal of the entire SCS system.

Care and Handling of Components. Use extreme care when handling system components prior to implantation. Excessive heat, excessive traction, excessive bending, excessive twisting, or the use of sharp instruments may damage a component, which may cause component failure.

Charging System Before Implant. To allow the surgical wound to heal before a charge is needed, verify that the IPG is fully charged before implanting. The charging paddle is not sterile, and contact with an unhealed wound may result in an infection.

Single-use, Sterile Device. The SCS system implanted components are single use only. Do not resterilize a system component or reimplant an explanted system component because of risk of infection or device malfunction.

Sterile Package or Component Damage. Do not implant a component if any of the following has occurred:

- The sterile package has been punctured or damaged, which may have compromised component sterility.
- The component shows evidence of damage, which may cause the component not to function properly.
- The IPG has been dropped on a hard surface, which may cause the IPG not to function properly.

Trial Cable. The trial cable is a single-use component; do not resterilize the trial cable because of risk of infection.

Use-by Date. Do not implant an SCS system component if the use-by date has expired. The use-by date is on the sterile package and the shelf carton. Return expired components to Nuvectra.

Other Medical Procedures and Therapies

System Interaction with Other Medical Treatments and Procedures. An IPG may interact with the following therapies or procedures:

- **Diagnostic ultrasound** (eg, carotid and Doppler scans) has no adverse effect on the IPG, leads, or extensions. The IPG may interfere with the scan by deflecting the ultrasonic beam.
- **Diagnostic x-rays.** The effects of diagnostic x-rays on an IPG are typically transient because interference occurs only during the time of x-ray exposure. In some cases, the IPG may need to be reprogrammed.
- **CT procedures.** For CT procedures on a patient with an implanted Algovita SCS System, the operator should:
  - » Ask the patient to use their programmer to turn the IPG off while the scan is performed, if possible.

- » Minimize x-ray exposure to the Algovita SCS System by:
  - » Using the lowest possible x-ray tube current consistent with obtaining the required image quality
  - » Making sure that the x-ray beam does not dwell over the device for more than a few seconds

Note: For CT procedures that require scanning over the medical device continuously for more than a few seconds, as with CT perfusion or interventional exams, attending staff should be ready to take emergency measures to treat adverse reactions if they occur.

After CT scanning, the operator should:

- » Ask the patient to use their programmer to turn the IPG back on if it was turned off prior to scanning
- » Advise the patient to contact their healthcare provider as soon as possible if they have questions or suspect their Algovita SCS System is not functioning properly after any medical procedure

The following therapies or procedures may turn stimulation off or may cause permanent damage to the IPG, particularly if used in close proximity to the IPG. These therapies or procedures may result in loss of therapy and additional surgery to remove or replace components of the Algovita SCS System.

- Radiotherapy
- Lithotripsy
- TENS unit
- External defibrillation
- Radiation therapy
- Ultrasonic scanning
- High-output ultrasound
- Transcranial magnetic stimulation (TMS)
- Electroconvulsive therapy (ECT)
- Magnetic resonance imaging (MRI) (Conditional for fully implanted system only)

If any of the therapies or procedures listed above are required by medical necessity:

- For MRI scans, all conditions in the Algovita SCS System MRI Procedure Guidelines must be met, and all instructions must be followed.
- For other therapies or procedures listed above:
  - » Put the IPG in storage mode by holding the Model 4900 Algovita Magnet over the IPG for more than 5 seconds.
  - » All equipment, including ground plates and paddles, must be used as far away from the IPG as possible.
  - » Every effort should be taken to keep fields, including current, radiation, or high-output ultrasonic beams, away from the IPG.
  - » Set equipment to the lowest energy setting clinically indicated.
  - » Following treatment, refer to the instructions provided in the Algovita Patient Magnet Manual, under the section, Bringing Your Stimulator Out of Storage Mode.
  - » Verify SCS system and therapy function.

Clinician Programmer, Programmer Charger, Pocket Programmer, and EPG

Charging Over an Unhealed Wound. Do not place the charging paddle on an unhealed wound. The charging paddle is not sterile, and contact with an unhealed wound may result in an infection.

Component Compatibility. Use only the programmers and accessories in the Algovita SCS System to charge and program the IPG, charge the programmers, or adjust stimulation. The effects of non-Algovita components on an Algovita SCS System are unknown.

Electromagnetic Interference (EMI). Do not use the Clinician Programmer near equipment that may generate electromagnetic interference. EMI may interfere with communication between the Clinician Programmer and other Algovita SCS System components. If EMI disrupts programming, move the Clinician Programmer away from the source of EMI. Examples of sources of EMI are magnetic resonance imaging (MRI), lithotripsy, computer monitors, cellular and cordless telephones, motorized wheelchairs, x-ray equipment, and other monitoring equipment. Interrupting programming may result in incorrect or incomplete programming.

Flammable Atmospheres

- Avoid using the Clinician Programmer, Patient Feedback Tool, or EPG in flammable or explosive environments (eg, an anesthetic mixture with air, oxygen, or nitrous oxide). Using a battery-powered device near flammable or explosive atmospheres can produce a spark which may cause injury.
- Advise patients to avoid using the Programmer Charger, Pocket Programmer, or EPG in flammable or explosive environments (eg, during vehicle refueling). Using a battery-powered device near flammable or explosive atmospheres can produce a spark which may cause injury.

Programmer Storage. If you store the Clinician Programmer, Programmer Charger, or Pocket Programmer for an extended period of time, make sure to periodically charge its battery. The programmers use a very small amount of battery charge while turned off and may become non-rechargeable if not periodically charged.

Patient Activities

Adverse Effects from Environmental Conditions. Advise patients to seek medical guidance before entering environments that could adversely affect the operation of the IPG or EPG.

To avoid adverse effects to the patient or damage to the IPG or EPG, patients should avoid:

- Areas protected by a warning notice preventing entry by patients who have a pacemaker implanted
- Extreme environmental temperatures

To avoid adverse effects to the patient or damage to the IPG, patients should avoid:

- Scuba diving below 5 meters (16 feet), hyperbaric chamber pressures exceeding 1.5 atmospheres absolute pressure, or other activities with large atmospheric pressure variations

Automobiles and Other Equipment. Advise patients to turn stimulation off before operating an automobile, other motorized vehicle, or potentially dangerous machinery or equipment. Sudden stimulation changes, if they occur, may distract patients from attentive operation of the vehicle or equipment.

Cell Phones. While interference with cell phones is not anticipated, cell phone technology continues to change, and interaction with an SCS system is possible. Advise patients to contact your office if they have a concern about cell phone interaction with their SCS system.

Manipulating the IPG. Advise patients not to rub or manipulate their IPG through the skin. Rubbing or manipulation can change the orientation of the IPG or flip the IPG over in their body. Manipulation can also cause damage to the system, lead dislodgement, skin erosion, or stimulation at the implant site. If the IPG flips, communication between the programmers and the IPG may be compromised and recharge time may be increased.

Postural Changes. Advise patients that changes in posture or abrupt movements may cause decreases, or uncomfortable or painful increases in the perceived stimulation level. Before making postural changes, or if unpleasant sensations occur while making postural changes, advise patients to turn their stimulation down or off.

Disposal

Explanted Component Disposal

Return explanted leads, extensions, IPGs, and anchors to Nuvectra. To permit analysis, do not autoclave the components or expose them to ultrasonic cleaning. Dispose of unreturned components according to local environmental regulations.

The IPG should be explanted before cremation and returned to Nuvectra. The cremation process may cause the IPG battery to explode.

Programmer Disposal

Algovita programmers contain rechargeable lithium batteries. Do not incinerate or dispose of the programmers in general household trash. When no longer needed, preferably return programmers to Nuvectra for proper disposal. Otherwise consult local regulations for proper disposal of electronic devices.

Individualization of Treatment

Patients achieve the best results when they are informed about the surgical procedure, therapy risks and benefits, self-care responsibilities, and follow-up requirements.

Patient Selection

Select patients carefully to ensure that:

- Their symptoms are of physiological origin
- They demonstrate the ability to properly operate the SCS system, including recharging the system on a recurring basis
- They are appropriate candidates for surgery
- They received satisfactory results from a stimulation trial

Long-term Effectiveness of Spinal Cord Stimulation

The long-term effectiveness of SCS systems has been documented. Long-term clinical data regarding the efficacy of Algovita SCS Systems is not yet available. Not all patients realize long-term benefits from SCS systems.

Adverse Events Summary

Potential risks resulting from a spinal cord stimulation implant procedure are similar to other spinal procedures and include the following:

- Temporary pain at the implant site, infection, cerebrospinal fluid (CSF) leakage and in rare circumstances, epidural hemorrhage, seroma, hematoma and paralysis.
- Patient use of anticoagulation therapies may increase the risk of procedure-related complications such as hematomas, which could produce paralysis.

Possible risks of having an implanted spinal cord stimulation system to treat pain include:

- Lead migration
- Allergic response or tissue reaction to the implanted system materials
- Hematoma or seroma at the IPG site
- Skin erosion at the IPG site
- Persistent pain at the IPG or electrode site

- Radicular chest wall stimulation
- Skin irritation at the IPG recharge site
- Loss of pain relief over time
- Uncomfortable stimulation or ineffective pain control caused by system issues due to random failure of the system components or battery, changes in electrode position, loose electrical connections, lead or extension insulation breaches or fractures
- Epidural Mass Formation at Lead. Over the course of months or years, permanent implantation of an SCS paddle lead or percutaneous lead can result in epidural mass formation around the lead, which could compress the spinal cord. The effect of spinal cord compression can range from muscle weakness to progressive quadriparesis. If a patient with an SCS lead presents with a new neurological deficit, spinal cord compression due to reactive tissue mass formation should be considered as a potential cause. If an epidural mass is identified in a patient who is asymptomatic, periodic monitoring should be considered.

For a comprehensive summary of adverse events, refer to the clinical summary.

Summary of Clinical Evaluation

The safety and effectiveness of the Algovita SCS System was based on a systematic review and meta-analysis of published clinical studies that evaluated the safety and/or effectiveness of fully implantable SCS systems in treating chronic intractable pain of the trunk and/or limb. The Algovita SCS System is similar in design, technology, performance, intended use, and patient population to the SCS systems evaluated in these studies. The literature review strategy was conducted according to the guidelines outlined in the PRIMSA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement[1].

A total of 23 studies with specific inclusion and exclusion criteria were identified by the meta-analysis for inclusion in the safety analysis. This resulted in 1670 patients implanted with SCS systems.

Five studies representing a total of 202 patients were included in the effectiveness analysis.

Objectives of Studies

Based on nonclinical studies that demonstrated that the Algovita device has comparable output characteristics to the commercially available SCS systems reported in the literature, the primary objective was to provide clinical evidence of the effectiveness of the Algovita device, using literature articles, for the relief of failed back surgery syndrome, intractable low back, and limb pain.

Effectiveness was demonstrated by 1) a reduction of pain as demonstrated by a significant reduction in the Visual Analog Scale (VAS) score, 2) a 50% reduction in pain using either a 3 or 4 point scale in at least 30% of patients included in that study, and/or 3) a significant difference in pain reduction as measured by a VAS score when compared to a control group.

Safety of the Algovita System was established using literature articles, for the relief of failed back surgery syndrome, intractable low back, and limb pain. This was accomplished by examining the incidence of complications of the SCS systems used in the published literature.

1 Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Summary of Literature Search Strategy

A literature search strategy consisted of seven primary steps:

1. Search of Medline database for indexed articles using MeSH terms (Medical Subject Headings, National Library of Medicine) relevant for SCS systems and treatment of trunk and/or limb pain (213 abstracts)
2. Search of non-indexed PubMed database using broad SCS terms (260 abstracts)
3. Identification of literature from other sources (4 abstracts)
4. Clinical review for inclusion by two independent reviewers using pre-defined criteria (79/477 abstracts selected)
5. Final selection of eligible articles by a clinical and statistical reviewer (27/79 articles)
6. Determination of studies with safety endpoints appropriate for the safety summary (23/27 studies)
7. Determination of studies appropriate for the efficacy summary (5/27), which required efficacy endpoints and excluded studies with (1) retrospective designs, (2) device features or waveforms not offered by Algovita, (3) subjects with ischemic pain, or (4) subjects with pain etiologies for which SCS has not demonstrated effectiveness such as CRPS I and diabetic neuropathy

Methods for Meta-Analysis

Safety Analysis

Standard summary statistics are provided for each adverse event type and surgical intervention. In cases where data for a particular event was reported in at least 4 studies, a random-effects model was used to estimate a pooled rate. Two additional models stratified by the ≤1 year time period and the >1 year time period were conducted if the event was reported by at least 4 studies in each time period. In the case the number of events was reported in the article, instead of the number of subjects experiencing an event, it was assumed that each event was experienced by a unique subject.

Efficacy Analysis

There were an insufficient number of studies to perform an efficacy meta-analysis, however a qualitative summary of efficacy findings for each eligible study is provided.

Evaluation of Safety

In total, 23 articles reported data on 20 subject populations (3 articles reported on the same subjects at later time point) which included a total of 1670 enrolled subjects eligible for inclusion in the qualitative safety review and meta-analysis. Of the 20 study populations, 8 were from retrospective case series, 7 from prospective case series, 2 from randomized trials, 2 from prospective studies, and 1 from a crossover trial.

Of the 20 study populations, the median sample size was 38 (range, 11 to 707), and 894 (53.5%) of the patients were female. The median average age was 52 years (range, 38 to 70). The median follow-up time was 2.0 years (range, 0.3 to 5.0). The studies enrolled patients between 1983 and 2010. Five of the 20 samples were patients from the United States, representing 921 (55.1%) of the subjects in the safety meta-analysis.

The safety profile based on adverse events reported for subjects with failed back surgery syndrome (FBSS) and chronic pain of the trunk and limbs.

Safety was assessed by analyzing the surgical interventions and adverse events reported in the clinical studies.

Surgical Interventions

Three categories of surgical intervention were analyzed:

- *System explant* was defined as definitive removal of the SCS system without subsequent replacement with a new system, which was typically associated with infection or inadequate pain relief.
- *System explant with replacement* was defined as temporary removal of the entire SCS system (ie, IPG and leads) with eventual replacement with a new system, which was usually secondary to an infection.
- *Revision* was defined as any surgical procedure required that did not involve complete explant of the system for adverse events such as lead failure/fracture, battery replacement, or IPG change-out.

A summary of the surgical intervention results is provided in *Table 2*.

Table 2. Results of Surgical Intervention Meta-Analysis

Procedure Type	N Samples (N Patients)[a]	N Interventions[b]	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR)[Range]
System explant (overall)	13 (1401)	62	2.7 (0.3 to 5.0)	5.2% (3.4 to 7.5)	6.2% (2.6 to 8.3) [0.0 to 16.7]
Explant with replacement (overall)	8 (284)	12	1.8 (0.9 to 5.0)	5.1% (2.6 to 8.2)	4.9% (4.1 to 5.9) [0.0 to 12.5]
Revision (overall)	18 (1395)	314	2.0 (0.3 to 5.0)	25.8% (13.7 to 40.1)	23.6% (11.8 to 36.5) [0.0 to 100]
Revision (≤1 year)	7 (340)	N/A	1.0 (0.3 to 1.0)	15.5% (7.3 to 26.1)	19.0% (10.8 to 25.9) [1.3 to 33.3]
Revision (>1 year)	13 (1143)	N/A	2.7 (1.1 to 5.0)	31.8% (15.4 to 50.9)	30.4% (12.5 to 41.7) [0.0 to 100]

a. Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 13 of the 20 total subject populations, comprising 1401 patients, had data for the outcome measure "System explant."

b. The number of interventions reflects the total number of interventions for the reported patient population. A patient may have experienced more than one intervention.

The reasons for system explant, system explant with replacement, and revision are summarized in *Table 3*, below.

Table 3. Summary of Reasons for Surgical Intervention

Reasons for Surgical Intervention[a]	N
System Explant (N=62)	
Infection	39
Lack of efficacy	6
Subject decision for morphine pump	3
Surgery	3
Reason unspecified	2
Allergy	1
Concomitant surgery	1
Dehiscence	1
Epidural abscess	1
Infection before permanent implant	1
Pregnancy	1
Recurrent rejection	1
Relapsing ulcerative colitis	1
Subject decision	1
System Explant with Replacement (N=12)	
Infection (including generator pocket infection)	9
Replacement of system (unspecified)	2
Skin problems at implant site	1
Revision (N=314)	
Lead migration	128
Lead connection failure	50
Lead repositioning	36
Lead fracture	35
Adverse event	11

Table 3. Summary of Reasons for Surgical Intervention	
Reasons for Surgical Intervention[a]	**N**
Pulse generator pocket	8
Inadequate paresthesia coverage	6
Lead replacement	6
Non-specific complications	5
Addition of second lead	4
Migration of electrodes and loss of paresthesia	4
Pain at incision site	4
Lead migration or lead added	3
Connection between lead and extension cable inadequate	2
Lead idiopathic failure	2
Lead repositioning due to technique issue	2
Loss of paresthesia	2
Defective lead	1
IPG migration	1
IPG repositioning	1
Lack of efficacy	1
Lead revision	1
Pocket revision	1

a. The reasons for surgical intervention are associated with the surgical interventions presented in the meta-analysis in *Table 2 on page 20*.

Adverse Events

In total, ten adverse event types had at least four reporting studies and were formally meta-analyzed: stimulation issues, pain over implant site, lead migration, ineffective pain control, lead fracture/failure, infection, skin erosion/problem at implant site, IPG malfunction, CSF leak, and seroma. *Table 4* shows an overall summary, sorted by the overall frequency of the adverse event.

Table 4. Summary of Meta-Analyzed Adverse Events

Adverse Event Type	N Samples (N Patients)[a]	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
Stimulation issue (overall)	4 (225)	1.0 (0.3 to 2.0)	41.1% (4.2 to 85.8)	25.2% (12.2 to 53.6) [11.9 to 100]
Pain over implant site (overall)	8 (1284)	2.0 (0.3 to 3.7)	29.2% (10.5 to 52.6)	9.7% (5.9 to 17.6) [0.8 to 95.5]
Pain over implant site (≤1 year)	5 (277)	0.9 (0.3 to 1.0)	8.3% (4.1 to 13.8)	6.1% (6.0 to 8.3) [5.3 to 21.4]
Pain over implant site (>1 year)	5 (1095)	2.0 (2.0 to 3.7)	22.3% (0.4 to 63.2)	11.9% (7.5 to 16.3) [0.8 to 95.5]
Lead migration (overall)	14 (1514)	2.0 (0.3 to 3.7)	10.2% (7.0 to 14.1)	8.0% (7.2 to 15.8) [2.4 to 25.0]
Lead migration (≤1 year)	7 (319)	1.0 (0.3 to 1.0)	9.3% (5.6 to 13.7)	9.1% (7.5 to 12.9) [2.4 to 25.0]
Lead migration (>1 year)	8 (1247)	2.9 (2.0 to 3.7)	10.7% (6.4 to 15.9)	7.8% (7.2 to 14.9) [4.3 to 22.6]
Ineffective pain control with permanent implant (overall)	6 (255)	2.0 (1.0 to 3.1)	9.4% (4.7 to 15.7)	11.5% (6.5 to 14.6) [2.4 to 22.2]
Lead fracture/failure (overall)	9 (1284)	2.7 (0.9 to 3.7)	5.7% (3.4 to 8.5)	7.1% (4.3 to 8.3) [1.9 to 25.0]
Lead fracture/failure (≤1 year)	4 (198)	1.0 (0.5 to 1.0)	3.7% (1.5 to 6.8)	3.3% (2.4 to 5.2) [2.4 to 8.2]
Lead fracture/failure (>1 year)	7 (1174)	3.1 (2.0 to 3.7)	6.0% (3.2 to 9.5)	7.1% (5.3 to 8.3) [1.9 to 25.0]
Infection (overall)	17 (1547)	2.0 (0.9 to 5.0)	5.3% (4.0 to 6.6)	6.1% (2.5 to 9.5) [0.0 to 12.5]

Table 4. Summary of Meta-Analyzed Adverse Events				
Adverse Event Type	**N Samples (N Patients)[a]**	**Median (Range) Follow-up Years**	**Pooled Rate (95% CI)**	**Median Rate (IQR) [Range]**
Infection (≤1 year)	6 (261)	1.0 (0.5 to 1.0)	6.3% (3.7 to 9.6)	6.5% (4.3 to 8.3) [2.4 to 12.5]
Infection (>1 year)	13 (1374)	2.7 (1.1 to 5.0)	5.2% (3.8 to 6.8)	6.1% (2.5 to 9.5) [0.0 to 11.1]
Skin erosion/problem at implant site (overall)	5 (515)	2.0 (0.3 to 3.7)	3.2% (0.6 to 7.7)	2.5% (2.4 to 3.6) [0.4 to 11.8]
CSF leak (overall)	4 (406)	1.0 (0.5 to 3.7)	3.0% (0.6 to 7.2)	4.3% (2.0 to 6.7) [0.8 to 8.3]
IPG malfunction (overall)	5 (484)	2.9 (0.9 to 3.7)	2.3% (0.7 to 4.7)	4.1% (2.4 to 4.8) [0.8 to 6.2]
Seroma (overall)	8 (1304)	2.6 (0.3 to 3.7)	1.4% (0.5 to 2.8)	1.4% (0.9 to 2.1) [0.0 to 7.1]

a. Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 4 of the 20 total subject population, comprising 225 patients, had data for the outcome measure "Stimulation issue."

All other adverse events had fewer than 4 studies reporting on the rate over follow-up. Therefore, each reported adverse event is summarized using standard summary statistics in *Table 5* below.

Table 5. Summary of Other Adverse Events

Adverse Event Type	N Studies (N Patients)[a]	Median (Range) Follow-up Years	Median Rate (IQR) [Range]
Allergy	1 (30)	1.6	3.4%
Bacterial meningitis	1 (30)	2.9	0.0%
Battery depletion	1 (84)	3.1	1.2%
CSF fistula	1 (260)	3.7	0.4%
Death (non-device related)	2 (289)	3.4 (3.0 to 3.7)	10.9% (9.5 to 12.4) [8.1 to 13.8]
Decubitus	1 (260)	3.7	3.8%
Disturbed urination	1 (36)	2.0	18.2%
Dysesthesia	1 (260)	3.7	0.4%
Epidural abscess	2 (278)	2.4 (1.0 to 3.7)	3.5% (2.1 to 4.9) [0.8 to 6.2]
External component failure	3 (194)	1.0 (0.9 to 3.1)	6.1% (3.7 to 6.6) [1.2 to 7.1]
Hematoma	2 (35)	3.1 (2.7 to 3.4)	2.2% (1.1 to 3.3) [0.0 to 4.3]
Hemorrhage (requiring surgery)	1 (260)	3.7	0.0%
Implant difficulty	1 (45)	1.0	4.8%
Implant technique complications	1 (52)	1.0	4.8%
Inflammation at implant site	1 (45)	1.0	11.9%
Lead revision	3 (118)	2.0 (1.6 to 5.0)	7.1% (5.3 to 39.0) [3.4 to 70.8]
Loose connection	2 (752)	2.2 (1.0 to 3.4)	8.3% (7.7 to 8.9) [7.1 to 9.5]
Lumbar site problem	1 (45)	1.0	4.8%

Table 5. Summary of Other Adverse Events			
Adverse Event Type	**N Studies (N Patients)[a]**	**Median (Range) Follow-up Years**	**Median Rate (IQR) [Range]**
Meningism	1 (260)	3.7	0.8%
More pain in other body parts	1 (36)	2.0	31.8%
Paraplegia	1 (260)	3.7	0.0%
Presumed epidural pneumocephalus headache	1 (260)	3.7	3.5%
Programming error	1 (45)	1.0	4.8%
Radiculopathy	1 (260)	3.7	0.8%
Recurrent rejection	1 (36)	5.0	4.2%
Revision of pulse generator pocket	1 (36)	5.0	33.3%
Spinal cord injury	1 (30)	2.9	0.0%
Ulcerative colitis	1 (36)	5.0	4.2%
Unable to operate patient programmer	1 (84)	3.1	3.6%

a. Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 1 of the 20 total subject population, comprising 30 patients, had data for the outcome measure "Allergy."

Evaluation of Efficacy

Five (5) articles from the systematic review of SCS systems reporting on four (4) subject populations (1 article reported on the same subjects at a later time point) were used to summarize the effectiveness of the Algovita SCS system (de Vos et al. 2012, Kumar et al. 2007, Kumar et al. 2008, Oakley et al. 2007, and Ohnmeiss et al. 1996). These studies included a total of 202 enrolled patients permanently implanted with a SCS system. These study populations were followed prospectively for a median of 1.5 years (range, 0.9 to 2 years), 119 (58.9%) were female, and the median average age was 51 years. The primary treated disease was failed back surgery syndrome or intractable lower extremity pain for all subjects. These characteristics are consistent with the patient population for which the Algovita SCS System is indicated.

- De Vos et al. (2012) conducted a prospective case series from 2008 to 2009 among 45 subjects (21 female) with a mean age of 56 years. Forty-two (42) subjects were ultimately implanted following test stimulation. At one year, the mean visual analog scale (VAS) score (on a scale of 0 to 10) for leg pain was significantly reduced from 8 to 3.2; the mean VAS score on lower back pain was also significantly reduced from mean of 7.5 to 4.2. The proportion of patients with a 50% or greater reduction in pain according to VAS was 71% for leg pain and 51% for back pain.
- Kumar et al. (2007) conducted a randomized controlled trial of SCS versus conventional medical management for failed back surgery syndrome (FBSS). The trial enrolled 100 subjects from 2003 to 2005 and reported six-month efficacy results. Forty-nine (49) subjects were female and the mean age was 50 years. Fifty-two (52) subjects were randomized to the SCS group and forty-eight (48) to the conventional medical management (CMM) group. Forty-eight (48) of the subjects randomized to the SCS group were ultimately implanted. At six months, 48% of SCS subjects had a 50% or greater reduction in leg pain compared to 9% in the CMM group; 22% of SCS subjects had an 80% or greater reduction in leg pain compared to 7% of subjects who received CMM. At six months, mean back and leg pain as measured by the VAS improved significantly greater among subjects in the SCS group than those who received CMM.
- Kumar et al. (2008) reported an update of the subjects randomized to receive SCS treatment for failed back surgery syndrome in the randomized controlled trial reported in Kumar et al. (2007). Forty-two (42) of the fifty-two (52) randomized subjects had two-year follow-up data. At two years, 69% had at least 30% leg pain relief, 40% had at least 50% leg pain relief, and 14% had at least 80% leg pain relief.

- Oakley et al. (2007) conducted a prospective trial of SCS in the US primarily among subjects with chronic, intractable pain of the trunk and/or limbs, primarily FBSS. Sixty-five (65) subjects (40% female) with a mean age of 52 years were enrolled between 2003 and 2004. Sixteen (25%) did not experience at least 50% pain relief with test stimulation and were not implanted. Due to the rolling enrollment, efficacy data were available for 47 subjects at 2 weeks, 38 at 3 months, 33 at 6 months, and 12 at 1 year, for a mean follow-up of 0.9 years among the 49 implanted subjects. The percentage of subjects reporting a 50% or greater improvement in pain was 85%, 63%, 55%, and 75% at each time point, respectively. The mean pain score as measured by the VAS (0-10 scale) was 8.0 baseline and was reduced to 2.5, 3.2, 3.9, and 2.2, respectively.
- Ohnmeiss et al. (1996) conducted a prospective study of SCS among subjects with intractable leg pain. In total, 40 subjects were implanted with a SCS system and were assessed at 6 weeks, 12 months, and 24 months post-implant. The baseline observation carried forward method was used to impute missing data for subjects with missing follow-up data in an intention-to-treat (ITT) analysis. Mean VAS scores for leg pain were 7.4 pre-operatively, and were reduced significantly to 4.2, 5.6, and 6.3 at 6 weeks, 12 months, and 24 months, respectively, in ITT analyses. At 24 months, leg pain, pain when walking, standing pain, pain's effect on lifestyle, and total VAS scores were significantly improved on average from pre-operative values.

Conclusions

The purpose of the systematic review was to summarize the safety and effectiveness of spinal cord stimulation therapy, using fully implantable stimulation (SCS) systems, in managing chronic intractable pain of the trunk and/or limbs. The safety meta-analysis included 23 studies with 20 subject populations (3 articles reported on the same subjects at later time points) and a total of 1670 subjects.

The findings with respect to surgical interventions demonstrated that revisions were the most common surgical intervention and occurred at 25.8%. Revisions were most often secondary to lead migration, followed by lead-related events, such as lead connection failure and lead fracture. Though smaller in number, IPG revisions required for battery replacement or IPG repositioning also contributed to the revision rate. System explants (without replacement), occurred at 5.2% and were typically due to infection, and to a lesser extent, inadequate pain relief. Finally, system explants (with replacement) occurred at 5.1% and were most often the result of infection.

The rates of occurrence for the ten adverse events appropriate for meta-analysis correspond to the surgical intervention rates determined by the meta-analysis: stimulation issues 41.1%, pain over implant site 29.2%, lead migration 10.2%, ineffective pain control with the permanent implant

9.4%, lead fracture/failure 5.7%, infection 5.3%, skin problems at the implant site 3.2%, CSF leak 3.0%, IPG malfunction 2.3%, and seroma 1.4%. In any cases where there was statistical evidence of publication bias, with one exception, the bias was in the more conservative direction where larger studies reported lower rates of adverse events than studies with smaller sample sizes.

The evaluation of efficacy was conducted using prospective studies relevant to Algovita SCS System features and indications. A total of five (5) studies based on 4 subject populations (1 article reported on the same subjects at a later time point) and 202 patients were qualitatively reviewed. The majority of patients had either intractable limb pain or FBSS and SCS treatment was demonstrated to be effective in each of the five studies.

Overall, the results of the systematic review and meta-analysis support the safety and effectiveness of SCS therapy in treating patients who suffer from chronic, intractable pain of the trunk and/or limbs. The Algovita System is similar to SCS systems approved by the FDA.

Note on Limitations of the Data

The data used to support the effectiveness of the Algovita device was based on literature studies. The studies were open label, in that patients knew they were receiving stimulation. Open label studies may cause an overestimation of the treatment effect in investigator and subject ratings. Also, open label studies do not assess the magnitude of the placebo response, regression to the mean, the effect of changes in medications or other treatments to alleviate pain or changes in the underlying severity of the pain disorder.

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Nuvectra Customer Service

If you have any questions about an Algovita SCS System, call Nuvectra Customer Service toll-free at 1-844-727-7897 within the United States. Outside of the United States, call your product distributor for assistance. If additional assistance is needed, contact Nuvectra Customer Service at +1-214-618-4980.

Component Compatibility

Only Algovita SCS System components should be used as part of an implanted Algovita SCS System.

Table 6. Algovita SCS System Component Compatibility

	Stimulator Model 2408 (3x8)	Extension Model 5208 (1x8)	Stimulator Model 2412 (2x12)	Extension Model 5212 (1x12)	Trial Stimulator Model 4300	Clinician Programmer Model 4500	Programmer Charger Model 4200	Pocket Programmer Model 4100
3x8 For Placing 1–3 8-electrode Leads								
Percutaneous Lead Models 1081-xx[1], 1084-xx, 1086-xx	■	■			■	■	■	■
Trial Lead Models 1081-xxT, 1084-xxT (Percutaneous)		■			■	■	■	■
2x12 For Placing 1–2 12-electrode Leads								
Percutaneous Lead Models 1121-xx, 1124-xx, 1126-xx			■	■	■	■	■	■
Paddle Lead Model 3000-xx (3-4-3-2)			■	■	■	■	■	■
Paddle Lead Model 3101-xx (2x6)			■	■	■	■	■	■
Trial Lead Models 1121-xxT, 1124-xxT (Percutaneous)				■	■	■	■	■

1. Denotes lead length

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