VNS Therapy™ System
Epilepsy Physician's Manual Australia (M1000)

SenTiva™ Generator—Model 1000

For Healthcare Professionals

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Australian Version

Rx Only

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For a list of symbols and glossary terms used with the VNS Therapy System, go to www.livanova.com.

1.1 Brief Device Description

1.1.1 The VNS Therapy System

The Model 1000 SenTiva™ generator is part of the LivaNova® VNS Therapy™ System, used for vagus nerve stimulation (VNS). The system consists of an implantable generator and lead; surgical accessories for implant; and external programming system used to change stimulation settings.

The Model 1000 is an implantable, multiprogrammable pulse generator that delivers electrical signals to the vagus nerve. It generator is housed in a hermetically sealed titanium case and is powered by a single battery. Electrical signals are transmitted from the generator to the vagus nerve by the lead.

The VNS Therapy Programming System includes a computer pre-installed with VNS Therapy programming software and a programming wand. Use the programming system to perform diagnostics, retrieve data and change settings.

1.2 Intended Use / Indications

The Model 1000 is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients 4 years of age and older with partial onset seizures (with or without secondary generalization) or generalized seizures that are refractory to antiepileptic medications.

This and other VNS Therapy devices may be approved for other indications in your market. All VNS Therapy labeling is located at www.livanova.com.

1.3 Contraindications

- **Vagotomy**—The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.
- **Diathermy**—Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as diathermy) on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

  Energy delivered by diathermy may be concentrated into or reflected by implanted products such as the VNS Therapy System. This concentration or reflection of energy may cause heating.

  Testing indicates that diathermy can cause heating of the VNS Therapy System well above temperatures required for tissue destruction. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve, tissue, or

vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

Because diathermy can concentrate or reflect its energy off any size implanted object, the hazard of heating is possible when any portion of the VNS Therapy System remains implanted, including just a small portion of the lead or electrode. Injury or damage can occur during diathermy treatment whether the VNS Therapy System is turned "ON" or "OFF."

Diathermy is further prohibited because it may also damage the VNS Therapy System components resulting in loss of therapy, requiring additional surgery for system explantation and replacement. All risks associated with surgery or loss of therapy (loss of seizure control) would then be applicable.

Advise your patients to inform all their healthcare professionals that they should not be exposed to diathermy treatment.

1.4 Warnings

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

1.4.1 All Devices

- **Use —** The VNS Therapy System should only be prescribed and monitored by physicians who have specific training and expertise in the management of seizures and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.
- **Not curative —** Physicians should warn patients that VNS Therapy is not a cure for epilepsy and that since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, and in strenuous sports that could harm them or others.
- **Unapproved uses —** The safety and efficacy of the VNS Therapy System have not been established for uses outside the "Intended Use / Indications" section, including (but not limited to) patients with:
    - Cardiac arrhythmias or other abnormalities
    - History of previous therapeutic brain surgery or CNS injury
    - History of dysautonomias
    - History of respiratory diseases or disorders, including dyspnea and asthma
    - History of ulcers (gastric, duodenal, or other)
    - History of vasovagal syncope
    - Only one vagus nerve
    - Other concurrent forms of brain stimulation
    - Pre-existing hoarseness

- Progressive neurological diseases other than epilepsy
- Under 4 years of age

- **Dysfunctional cardiac conduction systems —** The safety and effectiveness of the VNS Therapy System in patients with predisposed dysfunction of cardiac conduction systems (re-entry pathway) have not been established. Evaluation by a cardiologist is recommended if the family history, patient history, or electrocardiogram suggests an abnormal cardiac conduction pathway. Serum electrolytes, magnesium, and calcium should be documented before implantation. Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.
- **Bradycardia or asystole during implantation** — It is important to follow recommended implantation procedures and intraoperative product testing described in the *Implantation Procedure* chapter. During the intraoperative System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

  Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. If a patient has experienced asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate during a System Diagnostics (Lead Test) at the time of initial device implantation, the patient should be placed on a cardiac monitor during initiation of stimulation.

  The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.
- **External defibrillation or cardioversion (electrical)** — These procedures may damage the generator, and can temporarily or permanently damage the nerve. Attempt to minimize current flowing through the generator and lead system by following these precautions:
  - Position defibrillation patches or paddles perpendicular to the generator and lead system, and as far from the generator as possible.
  - Use the lowest clinically appropriate energy output (watt-seconds).
  - Confirm generator function after any internal or external defibrillation, or cardioversion treatment.
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Magnetic resonance imaging (MRI) — Patients with the VNS Therapy System, or any part of the VNS Therapy System, implanted should have MRI procedures performed **only as described in the *MRI with the VNS Therapy System* instructions for use**. In some cases, surgery will be required to remove the VNS Therapy System if a scan using a transmit RF body coil is needed.

- **Excessive stimulation—**Excessive stimulation is the combination of an excess duty cycle (i.e. one that occurs when ON time is greater than OFF time) and high frequency stimulation (i.e. stimulation at ≥ 50 Hz). Excessive stimulation has resulted in degenerative nerve damage in laboratory animals. Furthermore, excess duty cycle can be produced by continuous or frequent magnet activation (> 8 hours). While LivaNova limits the maximum programmable frequency to 30 Hz, it is recommended that you do not stimulate with excess duty cycle. Further, physicians should warn patients about continuous or frequent magnet use as this could lead to early battery depletion.
- **Device manipulation —** Patients who manipulate the generator and lead through the skin (Twiddler's Syndrome) may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve. For patients with the Model 1000, recalibration of Prone Position detection may be required. Patients, parents and caregivers should be warned against manipulating the generator and lead.
- **Swallowing difficulties —** Difficulty swallowing (dysphagia) may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Patients with pre-existing swallowing difficulties and those with a history of drooling or hypersalivation are at greater risk for aspiration. Appropriate aspiration precautions should be taken for such patients. Use of the magnet to temporarily stop stimulation while eating may mitigate the risk of aspiration.
- **Dyspnea or shortness of breath —** Dyspnea (shortness of breath) may occur with active VNS Therapy. Any patient with underlying pulmonary disease or insufficiency, such as chronic obstructive pulmonary disease or asthma, may be at increased risk for dyspnea and should have their respiratory status evaluated prior to implantation and monitored following initiation of stimulation.
- **Obstructive sleep apnea —** Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or prolonging "OFF" time may prevent exacerbation of OSA. Vagus nerve stimulation may also cause new onset sleep apnea in patients who have not previously been diagnosed with this disorder. It is recommended that patients being considered for VNS Therapy who demonstrate signs or symptoms of OSA, or who are at increased risk for developing OSA, should undergo the appropriate evaluation(s) prior to implantation.
- **Device malfunction —** Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause nerve damage and other associated problems. Patients should be instructed to use the magnet to stop stimulation if they suspect a malfunction, and then to contact their physician immediately for further evaluation. Prompt surgical intervention may be required if a malfunction occurs.
- **Sudden unexpected death in epilepsy (SUDEP) —** Through August 1996, 10 sudden and unexpected deaths (definite, probable, and possible) were recorded among the 1,000 patients implanted and treated with the VNS Therapy device. During this period, these patients had accumulated 2,017 patient-years of exposure.

  Some of these deaths could represent seizure-related deaths in which the seizure was not observed, at night, for example. This number represents an incidence of 5.0 definite, probable, and possible SUDEP deaths per 1,000 patient-years.

Although this rate exceeds that expected in a healthy (nonepileptic) population matched for age and sex, it is within the range of estimates for epilepsy patients not receiving vagus nerve stimulation, ranging from 1.3 SUDEP deaths for the general population of patients with epilepsy, to 3.5 (for definite and probable) for a recently studied antiepileptic drug (AED) clinical trial population similar to the VNS Therapy System clinical cohort, to 9.3 for patients with medically intractable epilepsy who were epilepsy surgery candidates.

1.4.2 Generators with the AutoStim Feature

Note: See "Features and Modes" section in Technical Information chapter for a full description of AutoStim Mode.

- **Cardiac arrhythmia —** The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias currently being managed by devices or treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillator, beta adrenergic blocker medications). Patients also should not have a history of chronotropic incompetence (commonly seen in patients with sustained bradycardia [heart rate < 50 bpm]).

  Note: See also "Effects on other medical devices" in the "Precautions" section of this chapter.

- **Pre-surgical Surface Assessment —** For anticipated use of the AutoStim feature, it is important to follow the recommended pre-surgical surface assessment described in the implantation procedure. For the device to detect heart rate, patients must have a peak-to-peak R-wave amplitude ≥ 0.4 mV on ECG measured from the proposed electrode location in the neck to the proposed generator location in the chest via surface ECG electrodes in the body positions described in the "Determine acceptable device implant locations" section of the *Implantation Procedure* chapter of this physician's manual.

1.4.3 Model 1000 (Serial Numbers <100,000 Only)

Some Model 1000 generators (serial numbers <100,000) report higher impedance values compared to prior models (Models 103-106), due to a change in the timing of the impedance measurement during the diagnostic test pulse. This timing difference will not impact the battery longevity or the ability to safely deliver therapy. However, it may result in an erroneous high impedance warning:

- **Potential erroneous high impedance warning during implantation surgery** — Erroneous high impedance is more likely for replacement generator surgeries compared to new implants due to fibrosis of the lead. Follow troubleshooting steps in the programming system physician's manuals to resolve common sources of true high impedance (confirm: lead pin insertion, setscrew tension, electrode placement on the nerve, irrigation of the nerve, and generator diagnostics indicative of normal function). If high lead impedance (≥ 5300 Ohms) is still reported, consider lead or generator replacement.

- **Potential erroneous high impedance warning at follow-up or titration visit** — If high lead impedance is observed (≥ 5300 Ohms,) perform a chest and neck x-ray (anteroposterior and lateral views) and contact Technical Support. Surgery is warranted if improper lead pin insertion or lead break is present in the x-ray. For implanted Model 1000 (serial numbers <100,000), advise patients to use the magnet daily to verify that stimulation is felt and report any change in perceived clinical symptoms related to stimulation (e.g., increase in seizures, painful stimulation, changes in perception of stimulation). In the absence of device-related complications (e.g. magnet stimulation is perceived and there are no changes in clinical symptoms), higher than expected lead impedance is not an indication of generator or lead malfunction. Continue to perform system diagnostics at each visit to monitor for further increases in impedance.

1.5 Precautions

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

1.5.1 General

- Unless otherwise specified, all indications, contraindications, and possible complications and adverse events are applicable to all implantable parts of the VNS Therapy System. Possible adverse events specifically related to the lead include migration, dislodgement, breakage, and corrosion.
- **Physician training** — Appropriate physician training is very important.
  - **Prescribing physicians** should be experienced in the diagnosis and treatment of epilepsy and should be familiar with the programming and use of the VNS Therapy System.
  - **Physicians who implant the VNS Therapy System** should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique relating to implantation of the VNS Therapy System.

    Note: See "Physician Training/Information" in the *Implantation Procedure* chapter.

- **Use during pregnancy —** The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. There are no adequate and well-controlled studies of VNS Therapy in pregnant women. Reproduction studies have been performed using female rabbits stimulated with the commercially available VNS Therapy System at stimulation dose settings similar to those used for humans. These animal studies have revealed no evidence of impaired fertility or harm to the fetus due to VNS Therapy. Because animal reproduction studies are not always predictive of human response and animal studies cannot address developmental abnormalities, VNS Therapy should be used during pregnancy only if clearly needed. Although the operating ranges of the VNS Therapy System and fetal monitors are dissimilar and no interaction would be expected, testing has not been performed. Therefore, the potential may exist for interaction between the VNS Therapy System and fetal monitoring systems.

- **Vagus nerve placement** — The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the **left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve.** The safety and efficacy of the VNS Therapy System have not been established for stimulation of the right vagus nerve or of any other nerve, muscle, or tissue.
- **Effects on other medical devices —**The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate device responses. If the patient requires concurrent implantable pacemaker, defibrillator therapy, or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device. Furthermore, when the VNS Therapy System and another stimulator are implanted in the same patient, the two stimulators should be placed at least 10 centimeters (4 inches) apart to avoid communication interference. Users should refer to the product labeling for the concurrent device to determine if there are additional precautions that should be observed.
- **Infection control** — It is important to follow infection control procedures. Infections related to any implanted device are difficult to treat and may require that the device be explanted. The patient should be given antibiotics preoperatively. The surgeon should ensure that all instruments are sterile prior to the operation. Frequent irrigation of both incision sites with generous amounts of bacitracin or equivalent solution should be performed prior to closure. To minimize scarring, these incisions should be closed with cosmetic closure techniques. Also, antibiotics should be administered postoperatively at the discretion of the physician. Children (4-11 years of age) may have a greater risk for infection when compared to adolescent and adult patients (≥12 years). Careful monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed.
- **Lead stabilization** — The patient can use a neck brace for the first week to help ensure proper lead stabilization.
- **Programming after surgery —** Do not program the VNS Therapy System to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation. Failure to observe this precaution may result in patient discomfort or adverse events.
- **Vagus nerve damage — Some complications** may be associated with damage to the vagus nerve.
    - Hoarseness may be caused by device malfunction, nerve constriction, or nerve fatigue. Nerve constriction should be apparent within a few days after implantation and may require explantation of the lead. Nerve fatigue usually occurs after intense stimulation parameters have been used, and might not be associated with any other adverse event. If fatigue is suspected, the generator should be turned off for several days until hoarseness subsides.
    - Persistent hoarseness *not* associated with stimulation suggests possible nerve irritation and should be immediately investigated.
    - Trauma to the vagus nerve at the implantation site could result in permanent vocal cord dysfunction.

- **Device reset** — A reset of the device will program the device OFF (output current = 0 mA).
- **Laryngeal irritation** — Laryngeal irritation may result from stimulation. Patients who smoke may have an increased risk of laryngeal irritation.

1.5.2 AutoStim Feature

- **Unintended Stimulation** — For devices that sense changes in heart rate, false positive detection may cause unintended stimulation. Examples of instances where heart rate may increase include exercise, physical activity, and normal autonomic changes in heart rate, both awake and asleep, etc. Depending on the amount of unintended stimulation, adjustments to the AutoStim feature's detection threshold should be considered. If necessary, the feature can be disabled.
- **Device Placement** — For the AutoStim feature, the physical location of the device critically affects its ability to properly sense heart beats. Therefore, care must be taken to follow the implant location selection process outlined in the *Implantation Procedure*. Note that this implant location selection procedure may be performed preoperatively as part of the patient's surgical work-up.
- **Battery Drain** — Talk to your patient about the AutoStim feature. Use of this feature will result in reduced battery longevity leading to more frequent replacements. Since the AutoStim feature can significantly affect the generator battery life, patients should return to their physician at appropriate intervals to evaluate whether they are receiving benefit from the current AutoStim settings.

Note: See the *Technical Information* chapter for more information.

1.5.3 Model 1000 Specific Features

Note: See the *Technical Information* chapter for a full description of the features below.

- **Low Heart Rate and Prone Position Detection**—These features are for informational purposes only. Do not use detected events for alarms or medical diagnosis.
- **Scheduled Programming** — Since this feature allows the generator to apply therapy increases at scheduled intervals, it may not be appropriate for use in patients who are nonverbal or are unable to use the patient magnet to stop undesired stimulation. Similarly, exercise caution for use of this feature in patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.
- **Day-Night Programming** — When using the optional Day-Night programming feature:
  - Consider risk and benefits of altering a patient's known efficacious settings before this feature is used or when parameter adjustments are made.
  - Inform your patients about when to expect a setting change (i.e., when Daytime settings transition into Nighttime settings).
  - Assess patient tolerability of the alternate parameter set before the patient leaves the office visit.

- **Time-based Features** — Day-Night Programming and Scheduled Programming do not automatically adjust for Day Light Savings or time zone changes. Tell the patient to follow-up with the physician for reprogramming, if needed.

1.5.4 Lead Evaluation and Connection

- **Do not use a lead other than** a VNS Therapy lead — Use a VNS Therapy dual-pin lead with the dual-receptacle generator or a VNS Therapy single-pin lead with the single-receptacle generator because use of other leads may damage the generator or injure the patient.
- **Lead size** —The lead is available in multiple sizes. Since it is not possible to predict in patients what size lead will be needed, it is recommended that at least one alternate lead size be available in the operating room. In addition, backups for leads should be available in the event of compromised sterility or damage induced during surgery.

  Note: For lead size availability, see "Lead Physical Characteristics" in the lead-specific *Technical Information* chapters.

- **Potential effects of lead breaks** — Lead fractures of the VNS Therapy System may prevent patients from receiving therapy. It may also prevent or interfere with tachycardia detection, if the feature is enabled. Children (4-11 years of age) may be more likely to exhibit certain risk factors for lead failures including a higher activity level and a higher likelihood to manipulate the lead. If a lead fracture is suspected, perform diagnostic testing to evaluate continuity within the system. If diagnostics suggest that a fracture is present, consider turning the VNS generator to zero milliamps (0 mA) of output current. Continuing stimulation with a fractured lead may result in dissolution of the conductor material resulting in adverse events, such as pain, inflammation, and vocal cord dysfunction. The benefits and risks of leaving the generator ON (actively stimulating) when a lead fracture is present should be evaluated and monitored by the medical professional treating the patient.

  Note: For more information on diagnostic testing, see "Troubleshooting" in this manual and in the programming system physician's manuals.

- **Line powered equipment** — Exercise extreme caution if testing the lead using **line-powered equipment** because leakage current can injure the patient.
- **Setscrew** — Do not insert a lead in the generator lead receptacle(s) without first visually **verifying that the setscrew(s) is sufficiently retracted** to allow insertion. Avoid backing the setscrew(s) out further than needed for lead insertion.
- **Hex screwdriver —** Ensure that the hex screwdriver is fully inserted in the setscrew, and then push in on the hex screwdriver and turn it clockwise until it clicks. To avoid damaging (stripping) the setscrew(s) and/or dislodging the setscrew plug(s), insert the hex screwdriver into the center of the setscrew plug, keeping it perpendicular to the generator.

1.5.5 Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal mode of operation.

1.5.5.1 Hospital and medical environments

- **VNS Therapy System operation should always be checked —** Perform device diagnostics after any of the procedures mentioned in this manual. Additional precautions for these procedures are described below.
- **Mammography —** For clear imaging, patients may need to be specially positioned for mammography procedures because of the location of the generator in the chest. (Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.)
- **Therapeutic radiation** — This procedure may damage the generator's circuitry. Sources of such radiation include therapeutic radiation, cobalt machines, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately.
- **Electrosurgery** — Use of electrosurgery (electrocautery or radio frequency [RF] ablation devices) may damage the generator. During the VNS implantation procedure, do not use electrosurgical equipment after the generator has been introduced to the sterile field. When performing other surgical procedures on a patient implanted with a VNS generator, attempt to minimize the current flowing through the generator and lead system by following these precautions:
  - Position the electrosurgery electrodes as far as possible from the generator and lead.
  - Avoid electrode placement that puts the generator or lead in the direct path of current flow or within the part of the body being treated.
  - Confirm that the generator functions as programmed after electrosurgery.
- **Electrostatic Discharge (ESD)** — ESD may damage the generator. Care should be taken when using the hex screwdriver to avoid touching the metal shaft when the screwdriver is engaged with the setscrew of the generator. This shaft can serve as a path to conduct electrostatic discharges into the device circuitry.
- **Extracorporeal shockwave lithotripsy** — This procedure may damage the generator. If therapeutic ultrasound is required, avoid positioning the area of the body where the generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the generator output to 0 mA for the treatment, and then after therapy, reprogram the generator to the original parameters.

- **Treatment involving electrical currents** — If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit), either the generator output should be set to 0 mA or function of the generator should be monitored during initial stages of treatment.
- **Therapeutic ultrasound —** Routine therapeutic ultrasound could damage the generator and may be inadvertently concentrated by the device, causing harm to the patient.
-  **Magnetic resonance imaging (MRI) —** An MRI should not be performed using a transmit RF body coil for certain VNS Therapy device configurations or under certain specific conditions. In some cases, heating of the lead caused by the transmit RF body coil during MRI may result in serious injury. Static, gradient, and radio frequency (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Magnet Mode output remains "ON".

  Note: See the *MRI with the VNS Therapy System* instructions for use for details.

-  **Receive RF coils** — Note that certain magnetic resonance (MR) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MR systems use a transmit/receive RF head coil. Local or surface coils may also be receive-only RF coils that require the transmit RF body coil for MRI. **The use of a receive RF coil does not alter hazards of the transmit RF body coil**.

  Note: See the *MRI with the VNS Therapy System* instructions for use for details.

-  **Transmit RF coils** — Exposure of the VNS Therapy System to any transmit RF coil must be avoided. Do not perform MRI scans using any transmit RF coil in the defined exclusion zones.
- **Routine diagnostic procedures** — Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.

1.5.5.2 Home occupational environments

- **Not expected to affect the generator** — Properly operating microwave ovens, electrical ignition systems, power transmission lines, theft-prevention devices, and metal detectors are not expected to affect the generator. However, because of their higher energy levels, sources such as transmitting antennas may interfere with the VNS Therapy System. It is suggested that the generator be moved away from equipment—typically at least 1.8 meters (6 feet)—that may be causing interference.

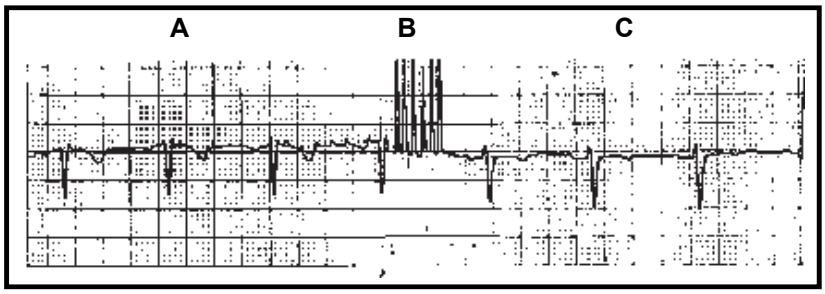
  Caution: The patient should seek medical advice before entering environments that are protected by a warning notice preventing entry by patients implanted with a cardiac pacemaker or defibrillator.

- **Cellular phones** — Based on testing to date, cellular phones have no effect on generator operation.
- **Electronic Article Surveillance (EAS) System tag deactivators —** EAS System tag deactivators can interfere with VNS Therapy when it's operated in proximity of the generator. Potential effects include inhibited pulses and accidental activations (Magnet or AutoStim). Patients should be cautioned to keep at least 60 centimeters (2 feet) away from EAS System tag deactivators to avoid potential interference.
- **Other Electro-mechanical devices** — Strong magnets, tablet computers and their covers, hair clippers, vibrators, loudspeaker magnets, and other similar electrical or electro-mechanical devices, which have a strong static or pulsing magnetic field, can cause accidental magnet activation. Patients should be cautioned to keep such devices at least 20 centimeters (8 inches) away from the generator.

1.5.5.3 Generator and EMI effects on other devices

- **Interference during stimulation** — During stimulation, the generator may interfere with devices operating in the 30 kHz to 100 kHz range (e.g., pocket transistor radios and hearing aids). This interference is a theoretical possibility, and no effects on hearing aids have been reported, although the generator can interfere with a transistor radio. No specific testing has been done to date, and no definite information on effects is available. The generator should be moved—typically at least 1.8 meters (6 feet)—away from equipment with which it may be interfering.
- **Interference during programming or interrogation** — Programming or interrogating the generator may momentarily interfere with other sensitive electronic equipment nearby. The generator is not expected to trigger airport metal detectors or theft-protection devices that are further than about 1.8 meters (6 feet).
- **Operation of other implanted devices** — The generator and the VNS Therapy magnet may affect the operation of **other implanted devices,** such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate generator responses. If the patient requires concurrent implantable pacemaker and/or defibrillator therapy, careful programming of each system is necessary to optimize the patient's benefit from each device.
- **Items affected by strong magnetic fields** — The magnet provided for activation or inhibition of the generator may damage **televisions, computer disks, credit cards, and other items** affected by strong magnetic fields.
- **Effects on ECG monitors** — Generator data communication produces an ECG artifact, an example of which is shown in the ECG tracings in Figure 1:

Figure 1. ECG Artifact Produced by Generator Communication



A Generator Off **B** Programming **C** Generator On

1.5.6 Sterilization, Storage, and Handling

1.5.6.1 Sterilization

The generator has been sterilized using hydrogen peroxide (H_2O_2 or HP) gas plasma and is supplied in a sterile pack to permit direct introduction into the operating field. An expiration (or use-before) date and method of sterilization is marked on each package.

■**Note**: A sterilization process indicator is located on the inner sterile pack and is only used as an internal manufacturing process aid.

Do not re-sterilize any VNS Therapy System product — Return any opened devices to LivaNova.

1.5.6.2 Storage

- **Store the VNS Therapy System** between - 20 °C (- 4 °F) and + 55 °C (+ 131 °F). Temperatures outside this range can damage components.
- **Do not store the VNS Therapy System** where it is exposed to water or other liquids. Moisture can damage the seal integrity of the package materials.
- **Nonpyrogenic** — The implantable portions of the VNS Therapy System are nonpyrogenic.

1.5.6.3 Handling

- **Do not implant a device** if any of the following has occurred:
  - The device has been dropped, because dropping it could damage internal components.
  - The outer or inner storage package has been pierced or altered, because this could have rendered it non-sterile
  - The expiration (use-before) date has expired, because this can adversely affect the device's longevity and sterility.
- **Do not ultrasonically clean the generator** — Ultrasonically cleaning the generator may damage generator components.

- **Do not reimplant an explanted generator** — The generator is a single-use-only device.
- **Do not reimplant an explanted generator for any reason**, because sterility, functionality, and reliability cannot be ensured, and infections may occur.
- **Return explanted devices** — Explanted generators should be returned to LivaNova for examination and proper disposal, along with a completed Returned Product Report form. Before returning an explanted device, disinfect Betadine®, Cidex® soak, or other similar disinfectant, and double-seal in a pouch or other container properly labeled with a biohazard warning.
- **Do not incinerate the generator —** The generator contains a sealed chemical battery, and an explosion could result if subjected to incineration or cremation temperatures.

1.6 Education, Training, and Services

LivaNova employs highly trained representatives and engineers located throughout the world to serve you and provide training to prescribers and implanters of LivaNova products. Physicians must contact LivaNova before prescribing or implanting a VNS Therapy System for the first time. In addition to the information provided in this physician's manual, training material includes but is not limited to, surgeon or prescribing physician training slide presentation, surgical video, training block & demo lead, etc. The required training (elements, duration, and frequency) to use LivaNova products may vary depending on the product and physician and can be discussed and arranged with your local LivaNova representative, or you can call or write LivaNova at the appropriate telephone number or address listed in the *Information and Support* chapter of this physician's manual to obtain more information.

2 Epilepsy Information—Clinical Studies

2.1 Clinical Studies—Safety

Note: For intended use/indications, see the *Introduction to the VNS Therapy System* chapter.

The VNS Therapy System was implanted in 454 patients in five clinical studies involving 611 devices (some patients had generator replacements). As of August 1996, total VNS Therapy exposure in these 454 patients was 901 device-years. Individual patient exposure averaged 24 months, with a range of eight days to 7.4 years.

A total of nine patients died during these five studies. One patient died from each of the following: thrombotic thrombocytopenic purpura, drowning, aspiration pneumonia, pneumonia, and renal failure associated with drug and alcohol ingestion. No cause of death was apparent for the other four deaths, which may be classified as sudden unexpected death in epilepsy (SUDEP). None of these deaths were attributed by the investigators to the VNS Therapy System.

2.1.1 Device Performance

The VNS Therapy System performed according to its specifications. Most device issues were communication difficulties resolved by repositioning the programming wand or replacing the programming wand batteries. One high lead impedance occurred requiring replacement; a lead break due to fatigue at the electrode bifurcation was noted. Most device complaints were resolved on the day of initial complaint.

2.1.2 Adverse Events Observed in Studies

Included among the five clinical trials were two randomized, blinded, active control trials (Study E03 and E05), which involved 314 patients and the implantation of 413 devices, yielding a total VNS Therapy System exposure (inclusive of long-term follow up) of 591 device years. These trials form the basis of the rates of observed adverse events.

Table 1 contains only a partial list of the more common and expected observed adverse events associated with the VNS Therapy System. A comprehensive listing of adverse events observed in studies is available by study from the Clinical Research department at LivaNova.

Table 1 reports the adverse events from these studies during the randomized phase (approximately a 14-week observation period) and randomized phase plus long-term follow up (> 3 months) through August 1996. The most common side effect associated with stimulation was hoarseness (voice alteration), which, depending on device settings, can be severe to barely perceptible. Hoarseness is reported to occur primarily during the ON period of stimulation.

Table 1. Observed Adverse Events

N=413 devices in 314 patients,152 patients in the HIGH treatment group, 591 device years						
	Randomized + Long-term Follow Up (> 3 Months) N=314 Patients, 591 Device-Years				Randomized Phase, HIGH Only, N=152 Pts	
Adverse Event (AE)	**Number of Patients***	**% of Patients†**	**Number of Events**	**Events/ Device-Year**	**Number of Patients**	**% of Patients**
Serious AEs‡						
Surgically related	13	4.1	13	0.022	N/A	N/A
Stimulation related	4	1.2	4	0.007	1	0.7
Non-serious AEs						
Voice alteration	156	50	720	1.228	91	60
Increased coughing	129	41	456	0.772	57	38
Pharyngitis	84	27	182	0.308	36	24
Paresthesia	87	28	377	0.638	32	21
Dyspnea	55	18	55	0.093	32	21
Dyspepsia	36	12	98	0.166	22	15
Nausea	59	19	154	0.261	21	14
Laryngismus	10	3.2	30	0.051	9	5.9

* Number of patients reporting the event at least once.

† Percentage of patients reporting the event at least once.

‡ Included infection, nerve paralysis, hypesthesia, facial paresis, left vocal cord paralysis, left facial paralysis, left hemidiaphragm paralysis, left recurrent laryngeal nerve injury, urinary retention, and low-grade fever.

2.1.2.1 Status epilepticus

Valid estimates of the incidence of treatment-emergent status epilepticus among VNS Therapy System treated patients are difficult to obtain because Investigators participating in clinical trials did not all employ identical rules for identifying cases. At a minimum, two of 441 adult patients had episodes that could be described unequivocally as "status." In addition, a number of reports were made of variably defined episodes of seizure exacerbation (for example, seizure clusters and seizure flurries).

2.1.2.2 Rebound after stimulation was stopped

Seizure frequency was monitored for one to four weeks after stimulation was stopped because of battery depletion in 72 instances (68 patients) in Study E03. Of these instances, 11 of the 72 (15%) **had a greater than 25 percent increase above baseline**, and 42 of the 72 (58%) had a greater than 25 percent decrease in seizure rate. The seizure rate increased by more than 1.5 standard deviations above baseline in 10 percent of instances (compared with the 7 percent expected).

2.1.3 Potential Adverse Events

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order:

- Ataxia (Loss of the ability to coordinate muscular movement)
- Dyspepsia (indigestion)
- Dyspnea (difficulty breathing, shortness of breath)
- Hypesthesia (impaired sense of touch)
- Increased coughing
- Infection
- Insomnia (inability to sleep)
- Laryngismus (throat, larynx spasms)
- Muscle movement or twitching generally associated with stimulation
- Nausea
- Pain
- Paresthesia (prickling of the skin)
- Pharyngitis (inflammation of the pharynx, throat)
- Voice alteration (hoarseness)
- Vomiting

Other potential adverse events possibly associated with surgery or stimulation include, but are not limited to, the following:

- Aspiration (fluid in the lungs)
- Blood clotting
- Choking sensation
- Damage to nerves or vasculature in the surgical area, including the carotid artery and jugular vein
- Device (generator and/or lead) migration or extrusion
- Dizziness
- Dysphagia (difficulty swallowing)
- Duodenal ulcer, gastric ulcer
- Ear pain
- Facial flushing (may be more likely in children aged 4-11 years)
- Facial paralysis, paresis
- Foreign body reaction to implants, including possible tumor formation
- Formation of fibrous tissue, pockets of fluid

- Heart rate and rhythm changes
- Hiccuping
- Incision site pain
- Irritability
- Laryngeal irritation (sore, painful throat)
- Left hemidiaphragm paralysis
- Left recurrent laryngeal nerve injury
- Left vocal cord paralysis
- Low-grade fever
- Muscle pain
- Neck pain
- Nerve injury
- Painful or irregular stimulation
- Seroma
- Skin, tissue reaction
- Stomach discomfort
- Tinnitus (ringing in the ears)
- Tooth pain
- Unusual scarring at the incision site
- Urinary retention
- Vagus nerve paralysis
- Weight change / Loss of appetite (potential for increased risk in children and adolescents)
- Worsening of asthma and bronchitis

⚠ **Caution:** Patients who manipulate the generator and lead through the skin may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve.

2.1.3.1 Analysis of Medical Device Reports submitted to the FDA—Epilepsy indication for the VNS Therapy System from July 1, 1997 through October 8, 2004

2.1.3.1.1. Summary

Once a medical device is approved for commercial distribution, the United States Food and Drug Administration (FDA) regulations require certain parties, including manufacturers of medical devices, to report to the FDA deaths and serious injuries to which a device has or may have caused or contributed. The required report is referred to as a medical device report (MDR).

As part of the approval for a new indication in 2005, the FDA Office of Biometrics and Surveillance analyzed all MDRs submitted for the VNS Therapy System from July 1, 1997 through October 8, 2004. During this period, the VNS Therapy System had a single approved indication, epilepsy. The analysis included 2,887 reports, 2,453 of which were reported from sites within the United States. By the end of the period analyzed, there were 32,065 VNS Therapy device implants and 80,144 device-years of implant experience. It is important to emphasize that, although the events occurred during treatment with the VNS Therapy System, the submission of an MDR does not necessarily mean the product caused or contributed to the event being reported.

2.1.3.1.2. Deaths

A total of 524 deaths were reported to the FDA during the period from July 1, 1997 through October 8, 2004. By the end of the period, there were 32,065 VNS Therapy device implants and 80,144 device-years of implant experience. Of the 524 deaths, 102 (20%) were of an "unknown cause," including 24 deaths of unknown cause that occurred during sleep (5% of total deaths). Of those deaths with a reported cause, the following were the most common etiologies:

- Seizure disorder (152 reports; 29% of total deaths), including sudden unexplained death in epilepsy and status epilepticus
- Respiratory events (99 reports; 19% of total deaths), including pneumonia, pulmonary edema, and hypoxia
- Cardiac events (51 reports; 10% of total deaths), including cardiopulmonary arrest, infarction, and arrhythmias
- Neurovascular events (24 reports; 5% of total deaths), including stroke and cerebral hemorrhage
- Malignancy (19 reports; 3% of total deaths), including brain and colon
- Suicide (9 reports; 2% of total deaths)

2.1.3.1.3. Serious injuries

A total of 1,644 serious injuries were reported to the FDA during the period from July 1, 1997 through October 8, 2004. By the end of the period, there were 32,065 VNS Therapy device implants and 80,144 device-years of implant experience. The most frequently reported serious injury was infection (525 reports). Approximately 40% of these were known to have required device explantation. The second most common serious injury reported was increased seizure activity (324 reports). Others included:

- Vagus nerve injury (181 reports), including vocal cord paralysis (109) and hoarseness (71)
- Respiratory injuries (141 reports), including sleep apnea (33), dyspnea (50), and aspiration (14)
- Cardiac events (123 reports), including tachycardia, bradycardia, palpitations, hypertension, hypotension, syncope, and asystole
- Pain (81 reports), including chest and neck pain
- Gastrointestinal events (60 reports), including dysphagia (24) and weight loss (24)

- Depression (21 reports)

Of the 1,644 reports of serious injury, 694 (42%) were associated with subsequent device explantation in that subject.

2.1.3.1.4. Device malfunctions

A total of 708 device malfunctions were reported to the FDA during the period from July 1, 1997 through October 8, 2004. By the end of the period, there were 32,065 VNS Therapy device implants and 80,144 device-years of implant experience. Some of the most common malfunctions reported were high lead impedance (351), lead breakage (116), device failure (44), and device migration (20).

2.2 Clinical Studies—Effectiveness

Five acute-phase clinical studies involving the VNS Therapy System have been conducted (see Table 2). These studies enrolled 537 patients, of whom 454 were implanted with the VNS Therapy System. A total of 611 devices were implanted, and patient exposure totaled 901 device-years, with an individual mean patient exposure of 24 months (ranging from eight days to 7.4 years). A total of 45 centers participated in these studies: 40 in the United States, 2 in Germany, and 1 each in Canada, Holland, and Sweden.

Note: References to "partial onset seizures" have been changed to "focal onset seizures" to align with updated official seizure type terminology; however, the functional definition of the condition remains the same.

Table 2. Description of Clinical Studies

All patients enrolled in all clinical studies, N=537						
Description of Clinical Studies						
	Longitudinal			**Parallel**		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
Type of study	pilot longitudinal	pilot longitudinal	open longitudinal	randomized parallel high/low	randomized parallel, high/low	-
Number of patients enrolled	11	5	133	126	262	537
Number of centers*	3	2	24	17	20	45
Reference period (baseline)	weeks 2 to 4	weeks 3 to 6	weeks -4 to 0	weeks -12 to 0	weeks -12 to 0	-
Seizure type	focal	focal	all types	focal	focal	-
Number of AEDs	1 to 2	1 to 2	not specified	0 to 3	1 to 3	-

* Total includes non-U.S. centers (Canada, Holland, Germany-2, and Sweden); several U.S. centers participated in more than one study.

2.2.1 Purpose

The purpose of the studies was to determine whether adjunctive use of optimal stimulation of the left vagus nerve could reduce seizure frequency in patients with refractory seizures.

2.2.2 Methods

In the two randomized, blinded, active control trials (E03 and E05), patients were randomly assigned to either of two treatment groups: HIGH (believed to be therapeutic) or LOW (believed to be less therapeutic). Patients enrolled in the study were seen every four weeks during the baseline period (weeks -12 to 0). Patients meeting eligibility were implanted with the generator and lead (see Table 3).

Two weeks after implantation, patients were randomized to the HIGH or LOW stimulation group, and the generator was activated. Patients in the HIGH groups received a higher frequency, greater pulse width, and higher duty cycle of stimulation. The randomized treatment period that followed activation of the generator lasted 14 weeks (the last 12 weeks of which were used in the efficacy analysis—the first two weeks for a treatment ramp-up period).

Table 3. Description of Patients

All patients implanted in all clinical studies, N=454						
Description of Patients						
	Longitudinal			**Parallel**		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
Number of patients implanted	11	5	124	115	199	454
Number of patients stimulated	10	5	123	115	198	451
Age in years (range)	32 (20–58)	33 (18–42)	24 (3–63)	33 (13–57)	33 (13–60)	32 (3–63)
Number of females (%)	4 (36%)	2 (40%)	57 (46%)	43 (37%)	104 (52%)	210 (46%)
Years with epilepsy (range)	22 (13-32)	20 (5-36)	17 (0.8-48)	21 (4-47)	23 (2-52)	21 (0.8-52)
Average number of AEDs	1.0	1.0	2.2	2.1	2.1	2.1
Median number of seizures per day at baseline	0.6	0.42	0.65	0.70 high/ 0.85 low	0.58 high/ 0.51 low	-

2.2.3 Results

The primary efficacy endpoint (percent reduction in seizure rate) was measured over 12 weeks (see Table 4). Adverse events were assessed at each patient visit.

Table 4. Principal Efficacy and Safety Results

All patients in efficacy analyses in all clinical studies, N=441						
Principal Efficacy Results						
	Longitudinal			**Parallel**		
Study	**E01**	**E02**	**E04**	**E03**	**E05**	**Total**
Number of patients in efficacy analysis	10	5	116	114	196	441
Median reduction in seizures/day	32%*	48%	22%*	23% high*/6% low	23% high†/21% low†	-
Mean reduction in seizures/day	24%‡	40%	7%‡	24% high‡/6% low	28% high†/15% low†	-
Difference in mean (high/low)	-	-	-	17%§ (3%/31%)	13%‖ (2%/23%)	-
% with > 50% response	30%	50%	29%	30% high/14% low	23% high/16% low	-
Principal Safety Results Through Long-term Follow Up						
Exposure (pt-yr)	45	20	245	456	135	901
SAEs¶	9%/ -	0%/ -	6%/ -	5%/0%	7%/9%	-
Discontinued (LOE/AE)#	0/1	0/0	2/3	0/2	1/3	3/9
Number of explants**	2	2	15	9	5	33
Deaths SUDEP/total††	0/0	0/0	3/4	0/3	1/2	4/9

Within group broad analyses:
* P ≤0.05, by Wilcoxon sign rank.
† P <0.0001, by anova.
‡ P ≤0.05, by Student's t-test.
Between group broad analyses:
§ P ≤0.02, by Wilcoxon rank sum; P ≤0.02, by Student's t-test.
‖ P <0.04, by aligned ranks test; P <0.02, by Student's t-test; P <0.03, by anova.
Safety information:
¶ SAEs = serious adverse events.
# Discontinuing for lack of efficacy (LOE)/adverse events (AE) at one year, excluding deaths.
** Number of explants through August 1996, excluding deaths.
†† All deaths occurred by the long-term follow-up closing date of August 1996.

Figure 2 and Table 5, which follow, show the results from Study E05, the largest and most recent of the randomized, blinded, active control studies:

Figure 2. Change in Seizure Frequency, Patient Distribution

(With Corresponding Table)
All E05 patients completing effectiveness evaluation, N=196

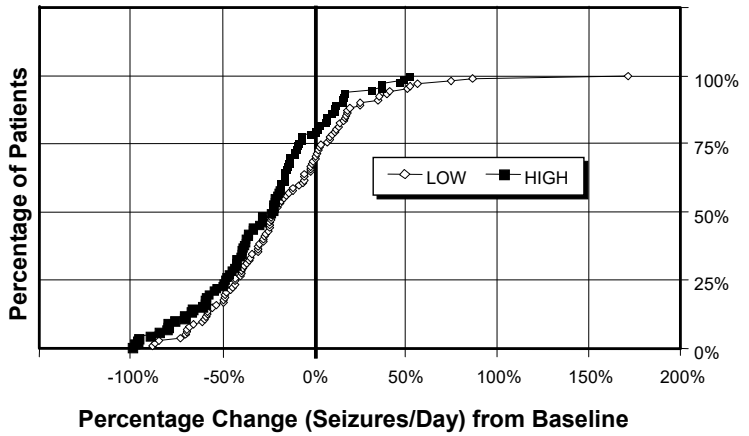


Table 5. Principal Effectiveness Statistics (E05)

All patients in E05 effectiveness analyses, N=196			
Percentage Change (Seizures/Day) from Baseline			
Statistics	**High (94)**	**Low (102)**	**Difference**
Median	-23%	-21%	N/A
25%, 75% Quartiles	-8.9%, -49%	4.0%, -43%	N/A
95% Confidence intervals	-35%, -21%	-23%, -7.7%	-23%, -2.3%
Range (min, max) Mean ± SD	-100%, 52%	- 89%, 171%	-23%, -2.3%
	-28% ± 34%	-15% ± 39%	-13%* ± 37%

* Difference is statistically significant (P <0.05) by analysis of variance (P=0.032) and by Cochran-Mantel-Haenszel aligned ranks (P=0.040).

Patient response to VNS Therapy was examined using statistical modeling (examining group characteristics) and an evaluation of individual patients. No useful predictors were found of an increase or a decrease in seizure frequency.

2.2.4 Conclusions

Patients with refractory focal onset seizures treated with HIGH VNS Therapy had a statistically significant decrease in frequency of seizures, compared with the baseline and compared with patients treated with LOW (active control) VNS Therapy. As indicated in Figure 2, most patients had a reduction in seizure frequency; some, however, had either no change or an increase in seizure frequency. The most common treatment-related adverse events were voice alteration and dyspnea. Treatment was well tolerated, with 97 percent (306 of 314) of the implanted patients continuing into the long-term follow-up phase of the study.

2.2.5 Long-term Data from Uncontrolled Follow Up

Long-term data (> 3 months' stimulation) were collected on all available E01 through E04 study patients (see Table 6). At the time the VNS Therapy System Premarket Approval Application was considered by the U. S. Food and Drug Administration, long-term data on most Study E05 patients were not available. These long-term follow-up data are uncontrolled because they come from an open-label protocol in which both the antiepileptic drug medications and the VNS Therapy device settings were allowed to be changed.

Ninety-five percent (95%) of patients were continuing one year after their original implant; 82 percent were still receiving stimulation at two years; and 69 percent were receiving stimulation at three years. Some E04 patients had not yet had the opportunity to reach two or three years of stimulation and therefore were not used in the calculations. Additionally, 28 E03 patients were implanted outside the United States in countries that later received commercial approval, and data were available through one year of stimulation only.

Table 6. Patient Summary Chart

Patients continuing treatment as of 8/22/96					
Study	**E01**	**E02**	**E03**	**E04**	**Total**
No. of patients randomized/ stimulated	10	5	115	123	253
No. of patients entering long-term phase	10	5	113	123	251
No. of continuing patients being treated for up to 1 year/ No. started	10/10	5/5	111/115	112/121*	238/251
No. of continuing patients being treated for up to 2 years/ No. started	9/10	4/5	71/87†	58‡/70	142/172
No. of continuing patients being treated for up to 3 years/ No. started	7/10	3/5	57/87	21§/24	88/126

* Two E04 Study patients had not been implanted long enough to reach the one-year date after implantation.

† Twenty-eight (N=28) commercial European patients were excluded from follow up after one year of treatment because of the commercial release of the VNS Therapy System in those countries.

‡ As of 8/22/96, only 70 patients had been implanted long enough to reach the two-year treatment period; 58 of the 70 were continuing.

§ As of 8/22/96, only 24 patients had been implanted long enough to reach the three-year treatment period; 21 of the 24 were continuing.

Table 7 shows the number of patients included in the efficacy analysis. It is apparent from the table that not all continuing patients were used in the efficacy analysis. This difference was mostly because of missing data (some patients kept only sporadic records over the long term), although two patients were not used because they had lobectomy surgery, which affected their seizure rates.

Table 7. Patients Used for Efficacy Analysis

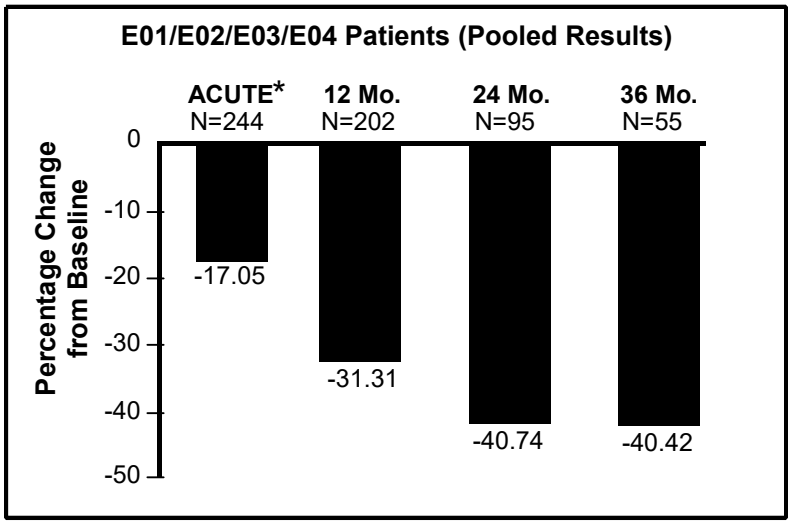
Study	E01	E02	E03	E04	Total
No. of patients randomized/stimulated	10	5	115	123	253
No. of patients entering long-term phase	10	5	113	123	251
No. of patients used in 1-year efficacy analysis/No. stimulated	10/10	4/5	102/111	86/112	202/238
No. of patients used in 2-year efficacy analysis/No. stimulated	8/9	2/4	51/71*	34/58†	95/142
No. of patients used in 3-year efficacy analysis/No. stimulated	4/7	2/3	49/57	0‡	55/67

* Of the 71 patients continuing, efficacy data were available for only 51.
† Of the 58 patients, efficacy data were available for only 34.
‡ No data were available at the three-year time for the E04 patients.

2.2.5.1 Long-term results

Available long-term data from uncontrolled, open-label protocols during which antiepileptic drug and VNS Therapy device setting changes were allowed suggest improved efficacy over the first 24 months of treatment, with stabilization of this improvement after two years (see Figure 3). As evident from Table 7, these long-term data are limited at years two and three, with no patients being represented in the three-year analysis from Studies E04 or E05. There can be no assurances that the efficacy of the VNS Therapy treatment will continue to improve or will not decline over time, nor can there be assurances that additional long-term data will not reveal new adverse information presently unknown to LivaNova. However, currently available long-term data do not suggest an increase or a worsening of adverse events, or a decline in efficacy.

Figure 3. Median Percentage Change in Seizure Frequency



* The acute phase results include seizure frequencies of the E03 Study LOW stimulation group, which included one-half the E03 patients, N=57. Patients were permitted to change their AEDs during these long-term follow-up studies, and these changes may have contributed to the change in seizure frequency.

2.2.5.2 Other information

Unlike the two randomized studies, Study E04, an open-label safety study, included patients 12 years old and younger, and patients with generalized seizures. Sixteen patients under age 12, ranging from 3.6 to 12 years old, were evaluated. (Two additional patients had unevaluable seizure data.) These patients were found to have a 17.9 percent median decrease in seizures during the acute phase, with 31 percent of the patients experiencing a greater than 50 percent decrease.

Additionally, 25 patients with generalized seizures were evaluated. (Two additional patients had unevaluable seizure data.) These patients were found to have a 46.6 percent median decrease in seizures during the acute phase, with 44 percent experiencing a greater than 50 percent decrease. The E04 results (N=116 analyzed), including patients younger than 12 and those with generalized seizures, showed a 22 percent median decrease during the acute phase, with 29 percent of the patients experiencing a greater than 50 percent decrease.

The E04 results (N=86 analyzed), excluding patients younger than 12 and those with generalized seizures, showed an 18.3 percent median decrease in seizures during the acute phase, with 27.9 percent of the patients experiencing a greater than 50 percent decrease.

2.2.5.3 Mechanism of action

The precise mechanism(s) by which the VNS Therapy System exerts its anticonvulsant action is unknown. In animal models designed to examine anticonvulsant activity, vagus nerve stimulation prevented seizures or seizure spread in these models: maximum electroshock (MES), pentylenetetrazol (PTZ) tests, 3-mercaptopropionic acid (3-MPA), alumina gel, potassium penicillin, strychnine, and kindling. With the exception of the alumina gel model, vagus nerve stimulation did affect the heart and respiratory rate, which may have contributed to the alteration in seizure activity.

Localization of vagus-initiated activity in the brain has been observed through animal studies of *fos*[1] immunoreactivity, regional brain glucose metabolism, and positron emission tomography (PET) imaging in human patients.

An [^{15}O] H_2O PET study in 10 patients demonstrated that vagus nerve stimulation by the VNS Therapy System does increase blood flow in the rostral medulla, right thalamus, and right anterior parietal cortex, and bilaterally in the hypothalamus, anterior insula, and inferior cerebellum. Decreases in blood flow were detected bilaterally in the hippocampus, amygdala, and posterior cingulate gyrus.

[1] *Fos* is a nuclear protein that is expressed under conditions of high neuronal activity.

2.3 Safety and Effectiveness in Pediatric Patients

Pre-market clinical and post-market surveillance data were used to extrapolate the safety and effectiveness of VNS Therapy from adolescents and adults (≥ 12 years) to children (4-11 years) to support the approval of VNS Therapy in patients 4-11 years of age.

2.3.1 Extrapolation Methods

Extrapolation is the leveraging process whereby an indication for use of a device in a pediatric population can be supported by existing clinical data from a studied population. Extrapolation of the safety and effectiveness of VNS Therapy for patients 4-11 years of age was conducted using a Bayesian hierarchical model to estimate the 50% responder rate in patients 4-11 years of age following 12 months of treatment utilizing existing clinical data across several data sources. Data from a prospective, open label, post-approval study of all consecutive patients treated with VNS Therapy in Japan was the primary data source. Historical data from E03, E04, E05, and E06 were used as prior data in the Bayesian model. The Bayesian hierarchical model borrows data from prior studies to the degree the current study data matches the previous studies' data.

2.3.2 Data Sources

The following data sources were included in the analysis:

- Pre-market data from the E03, E04, and E05 clinical trials
- E06: Randomized, parallel group, comparative study to compare the efficacy of VNS Therapy to antiepileptic drug (AED) treatment in reducing the frequency of seizures in children (age 17 or less). The study was initiated in October 2004 and completed in January 2010.
- Japan Post-Approval Study (PAS): Prospective, open label, post-approval study of all consecutive patients treated with VNS Therapy in Japan. Patients were implanted between July 2010 and December 2012.
- LivaNova Post-Market Surveillance Database: Passively reported adverse events and device tracking data from patients implanted with the VNS Therapy System from November 1988 to September 2015. When assessing device relatedness, post-market data was restricted to reports starting in November 2006 when the post-market coding system was updated to include device relatedness.

2.3.3 Data Sets Analyzed

The safety population included all patients 4 years of age and older who underwent implantation with the VNS Therapy System who:

- participated in the E03, E04, E05, or E06 clinical trial,
- participated in the Japanese PAS (initial implants only), or
- had a record in the LivaNova Post-Market Surveillance database.

Clinical study data from 847 patients were included in the safety population. Of these, 13.8% (n=117) of patients were 4-11 years of age, 23.5% (n=199) of patients were 12-21 years of age, and 62.7% (n=531) were > 21 years of age. Post-market surveillance data with information on device relatedness for adverse events were available from 40,926 patients. Of these 18.9% of

patients were 4-11 years (n=7,729), 22.9% (n=9,389) of patients were 12-21 years of age, and 58.2% (n=23,808) were > 21 years of age.

Patients in the efficacy population included all patients in the safety population with refractory focal onset seizures who had at least 1 seizure recorded at baseline. Patients who were only in the post-market surveillance database were excluded from the efficacy analysis. In total, clinical study data from 663 patients were included in the efficacy analysis. Of these, 582 patients had 12-month efficacy outcome data (n=54 patients 4-11 years, n=126 patients 12-21 years, and n=402 patients > 21 years of age).

Pediatric patients under 12 years of age participated in the E04, E06, and Japan PAS. The E03 and E05 studies consisted of patients > 12 years of age. Baseline characteristics by age group are reported in Table 8. Both groups had similar rates of prior brain or epilepsy surgery (35.0% of patients 4-11; 34.3% of patients ≥ 12), however pediatric patients 4-11 years of age in the safety population were more likely to have only generalized seizures (49.6% of patients 4-11; 16.2% of patients ≥ 12 years). Note that the efficacy evaluation is limited to patients with focal onset seizures.

Table 8. Demographics (Safety Population)

	4-11 Years	≥ 12 Years	Overall
Gender [n=(%)]			
N	117	730	847
% Female	45.3% (53/117)	44.1% (322/730)	44.3% (375/847)
Age (years)			
N	117	730	847
Average ± SD (Range)	8.4 ± 2.2 (4.0-11.9)	30.6 ± 11.5 (12.0-73.0)	27.6 ± 13.2 (4.0-73.0)
Age at Epilepsy Onset (years)			
N	117	719	836
Average ± SD (Range)	1.7 ± 1.9 (0.0-7.8)	10.5 ± 10.6 (0.0-63.7)	9.2 ± 10.4 (0.0-63.7)
Time to VNS Since Diagnosis (years)			
N	117	719	836
Average ± SD (Range)	6.7 ± 2.5 (1.2-11.6)	20.1 ± 10.6 (0.1-61.0)	18.2 ±10.9 (0.1-61.0)
Prior Brain or Epilepsy Surgery			
N	117	727	844
% Prior Surgery	35.0% (41/117)	34.3% (249/727)	34.4% (290/844)
Baseline Seizure Type			
N	117	730	847
Focal Onset	49.6% (58/117)	83.7% (611/730)	79.0% (669/847)
Generalized Only	49.6% (58/117)	16.2% (118/730)	20.8% (176/847)
Zero Baseline Seizures	0.9% (1/117)	0.1% (1/730)	0.2% (2/847)

2.3.4 Primary Endpoints

2.3.4.1 Primary Safety Endpoint

The primary safety endpoint was the incidence rate of device-related treatment emergent adverse events through 12 months of treatment. Adverse event rates for patients 4-11 years were compared to that of patients 12-21 years (comparable with respect to physiological development) via a 95% confidence interval for the incidence rate ratio. Adverse events with statistically significant incidence rate ratios greater than 1 indicate that the incidence rate for patients 4-11 years of age is greater than the incidence rate for patients 12-21 years of age. This analysis was performed separately for the shorter-term clinical study data and the longer term, larger post-market surveillance data to assess consistency of results.

2.3.4.2 Primary Efficacy Endpoint

The primary effectiveness endpoint is the proportion of patients 4-11 years of age in the Japan PAS with at least a 50% reduction in the frequency of seizures following 12 months of treatment. The pre-established efficacy threshold was set to a 30% responder rate with a corresponding 10% non-inferiority (NI) margin. A Bayesian hierarchical model was used to model the 12-month rates for each study.

2.3.5 Safety

Based on the clinical data, the overall incidence rate of device related treatment emergent adverse events was not different for patients 4-11 years of age compared to patients 12-21 years of age (Incidence Rate Ratio (IRR): 0.44, 95% CI: 0.20, 1.04). There were no device-related treatment emergent adverse events that had a statistically higher incidence rate in the 4-11 year age group when compared to 12-21 year age group. Two adverse events, myalgia and paresthesia, had statistically lower incidence rates in the 4-11 age group when compared to the 12-21 age group (Table 9).

Table 9. Primary Safety Analysis (Clinical Data)

Device-Related, Treatment-Emergent Adverse Events by Age based on Clinical Data (overall and statistically significant differences)					
Adverse Event	**4-11 years (N=117 patients, 113 person years)**		**12-21 years (N=199 patients, 194 person years)**		**Incidence Rate Ratio* (IRR) (95% CI)**
	Number of AE Reports	**Incidence Rate/PY (95% CI)**	**Number of AE Reports**	**Incidence Rate/PY (95% CI)**	
Overall Rate	**75**	**66.6% (32.2%-145%)**	**293**	**151% (109%-207%)**	**0.44 (0.20-1.04)**
Statistically Significant Difference in Incidence Rates (IRR <1)					
Myalgia	1	0.9% (0.0%-5.4%)	11	5.7% (0.0%-33.8%)	0.16 (0.00-0.90)
Paraesthesia	1	0.9% (0.0%-5.1%)	23	11.9% (5.8%-22.1%)	0.07 (0.00-0.79)

Based on post-market surveillance data, the overall incidence rate of device related treatment emergent adverse events was lower for patients 4-11 years of age compared to patients 12-21 years of age (IRR: 0.82, 95% CI: 0.77, 0.88) (Table 10). Infection and extrusion of lead had a statistically greater incidence rate in patients 4-11 years of age. Younger patients may have a greater risk for wound infection when compared to adolescent and adult patients; therefore, the importance of monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed.

Table 10. Primary Safety Analysis (Post-Market Data)

Device-Related, Treatment-Emergent Adverse Events by Age based on Post-Market Data (overall and statistically significant differences)							
Adverse Event	**4-11 years (N=7,729 patients, 31,220 person years)**			**12-21 years (N=9,389 patients, 37,647 person years)**			**Incidence Rate Ratio (95% CI)**
	Number of AE Reports	**Incidence Rate / Person Year (95% CI)**	**% of Total Reports**	**Number of AE Reports**	**Incidence Rate / Person Year (95% CI)**	**% of Total Reports**	
Overall	**1328**	**4.25% (4.03%, 4.49%)**	**100%**	**1948**	**5.17% (4.95%, 5.41%)**	**100%**	**0.82 (0.77, 0.88)**
Statistically Significant Difference in Incidence Rates (IRR > 1)							
Infection	85	0.27% (0.22%, 0.34%)	6.40%	67	0.18% (0.14%, 0.23%)	3.44%	1.53 (1.11, 2.11)
Extrusion of Lead	15	0.05% (0.03%, 0.08%)	1.13%	5	0.01% (0.00%, 0.03%)	0.26%	3.62 (1.31, 9.95)
Statistically Significant Difference in Incidence Rates (IRR < 1)							
Painful Stimulation	83	0.27% (0.21%, 0.33%)	6.25%	200	0.53% (0.46%, 0.61%)	10.27%	0.50 (0.39, 0.65)
Pain	60	0.19% (0.15%, 0.25%)	4.52%	150	0.40% (0.34%, 0.47%)	7.70%	0.48 (0.36, 0.65)
Voice Alteration	66	0.21% (0.16%, 0.27%)	4.97%	122	0.32% (0.27%, 0.39%)	6.26%	0.65 (0.48, 0.88)
Stimulation Not Perceived	37	0.12% (0.08%, 0.16%)	2.79%	99	0.26% (0.21%, 0.32%)	5.08%	0.45 (0.31, 0.66)
Coughing	47	0.15% (0.11%, 0.20%)	3.54%	88	0.23% (0.19%, 0.29%)	4.52%	0.64 (0.45, 0.92)
Migration of Generator	12	0.04% (0.02%, 0.07%)	0.90%	48	0.13% (0.09%, 0.17%)	2.46%	0.30 (0.16, 0.57)
Dysphagia	14	0.04% (0.02%, 0.08%)	1.05%	40	0.11% (0.08%, 0.14%)	2.05%	0.42 (0.23, 0.78)
Cognitive Changes	16	0.05% (0.03%, 0.08%)	1.20%	35	0.09% (0.06%, 0.13%)	1.80%	0.55 (0.31, 1.00)
Erratic Stimulation Perceived	4	0.01% (0.00%, 0.03%)	0.30%	15	0.04% (0.02%, 0.07%)	0.77%	0.32 (0.11, 0.97)
Continuous Stimulation Perceived	3	0.01% (0.00%, 0.03%)	0.23%	13	0.03% (0.02%, 0.06%)	0.67%	0.28 (0.08, 0.98)
Syncope	1	0.00% (0.00%, 0.02%)	0.08%	11	0.03% (0.01%, 0.05%)	0.56%	0.11 (0.01, 0.85)

2.3.6 Efficacy

Baseline seizure frequency for patients in the ITT population with 12-month efficacy data by age group is reported in Table 11. The median baseline seizure rate per month across all studies is 21.3 seizures/month. The median baseline seizure rate for patients 4-11 years of age (85.7 seizures/month) was higher when compared to adolescent and adult patients (30.4 and 17.4 seizures/month, respectively). Due to the differences in baseline seizure frequency rates by age group, this variable was evaluated as potential covariate in the hierarchical model; however, there was no evidence that baseline seizure frequency is associated with the probability of being a responder (% seizure reduction ≥ 50%).

Table 11. Baseline Seizure Frequency

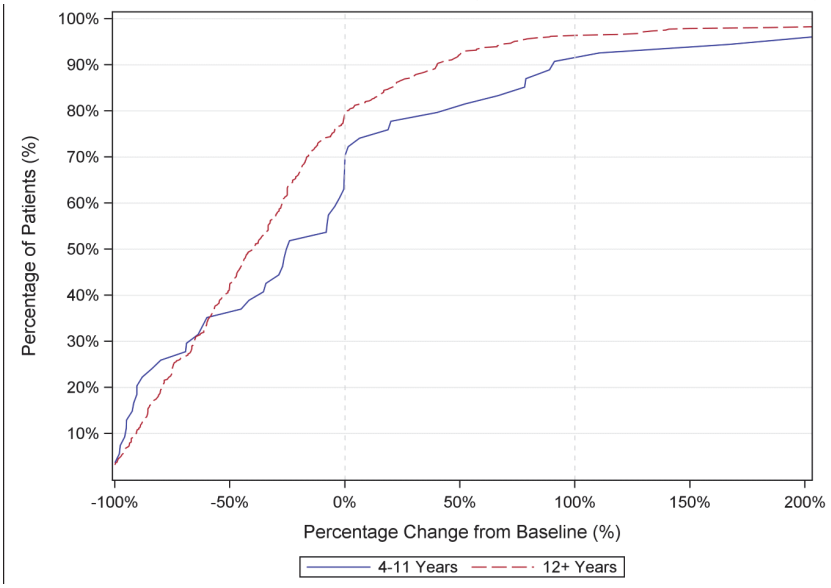
Baseline Seizure Frequency Per Month				
Age Group	**4-11 Years**	**≥12 Years**		**Overall**
N	54	528		582
Median	85.7	19.5		21.3
Age Group	**4-11 Years**	**12-21 Years**	**≥22 Years**	**Overall**
N	54	127	401	582
Median	85.7	30.4	17.4	21.3

Median percent reduction in seizure frequency from baseline to 12 months by age category is reported in Table 12. Following 12 months of treatment, there was no statistically significant difference in the median percent seizure reduction when comparing patients 4-11 years (-24.7%) with patients > 12 years of age (-40.4%) (p=0.142). Figure 4 shows the cumulative change in seizure frequency following 12 months of treatment for the ITT population by age group (4-11, ≥ 12 years).

Table 12. Median Percent Change in Seizure Frequency

Median percent change in seizure frequency at 12 months, by age group		
Age Group	**4-11 Years**	**> 12 Years**
N	54	528
Median	-24.7%	-40.4%
95% CI	-45.1% to 0%	-45.6 to -33.3%
p-value, Mann-Whitney	0.142	

Figure 4. Change in Seizure Frequency, Patient Distribution by Age Group



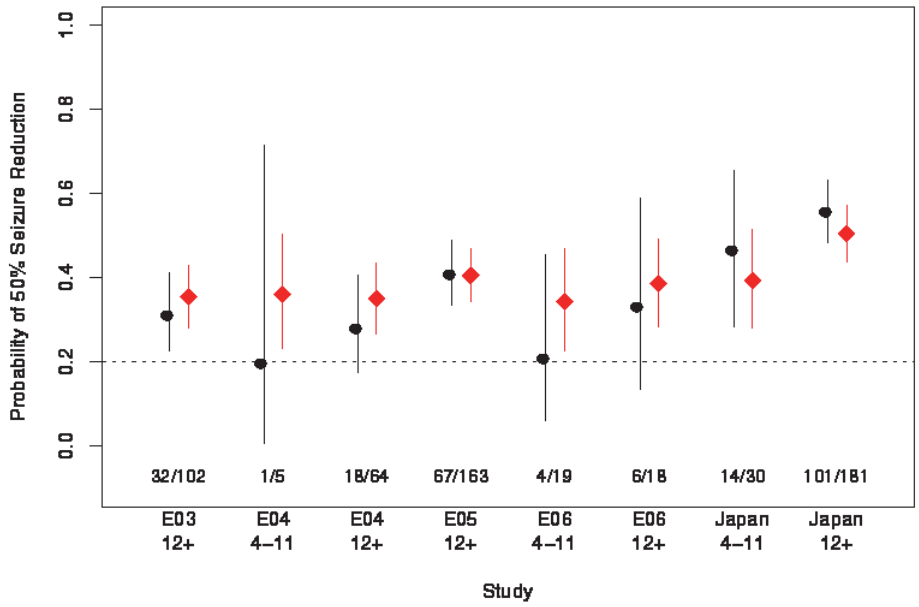
The Bayesian hierarchical model, which borrows from previous study data, estimated the 12 month responder rate for patients 4-11 years of age with focal onset seizures in the Japan PAS as 39% (95% credible interval: 28%, 52%). Since the entire 95% credible interval is greater than 20%, the primary efficacy endpoint was met. Across all studies, the Bayesian hierarchical model estimate for responder rate in patients 4-11 years of age is 37% (95% credible interval: 26%, 48%). (Table 13, Figure 5).

Table 13. Primary Efficacy Analysis

50% Response Rates at 12 Months						
Study	**Age Group**	**Responders**	**Frequentist Estimate**	**95% Exact Binomial CI**	**Bayesian Estimate**	**95% Credible Interval**
E-03	12+	32/102	31%	23-41%	35%	28-43%
E-04	4-11	1/5	20%	1-72%	36%	23-50%
E-04	12+	18/64	28%	18-41%	35%	27-44%
E-05	12+	67/163	41%	33-49%	41%	34-47%
E-06	4-11	4/19	21%	6-46%	34%	23-47%
E-06	12+	6/18	33%	13-59%	39%	28-49%
Japan	**4-11**	**14/30**	**47%**	**28-66%**	**39%**	**28-52%**
Japan	12+	101/181	56%	48-63%	50%	44-57%
Overall	4-11	19/54	35%	23-49%	37%	26-48%
Overall	12+	224/528	42%	38-47%	39%	33-46%

Note: VNS may be less effective in children who have previously undergone epilepsy surgery.

Figure 5. Probability of ≥ 50% Seizure Reduction at 12 Months



Frequentist (black), Bayesian (red)

2.3.7 Overall Study Conclusions

The results of the extrapolation study demonstrate that VNS Therapy is a safe and effective treatment for the reduction of focal onset seizures in pediatric patients 4-11 years of age with refractory epilepsy. Based on the Bayesian hierarchical model, the 12 month responder rate for pediatric patients 4-11 years of age with focal onset seizures in the Japan PAS is 39% (95% credible interval: 28%-52%). There were no unanticipated adverse device effects observed in pediatric patients 4-11 years of age. However, infection and extrusion of lead had a statistically greater incidence rate in patients 4-11 years of age. Younger patients may have a greater risk for wound infection when compared to adolescent and adult patients; therefore, the importance of monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed. Otherwise, treatment-emergent adverse events in patients 4-11 years of age were consistent with patients ≥ 12 years of age treated with VNS Therapy and no new risks were identified.

2.4 Bibliography

A bibliography of animal and clinical studies is available from LivaNova on request.

3 Technical Information — Model 1000 Generator

3.1 Detailed Device Description

3.1.1 Physical Characteristics

The titanium case of the Model 1000 generator is hermetically sealed and leak-rate tested. Specially designed feedthrus using platinum conductors form the electrical connection from the connector blocks to the circuitry through the hermetically sealed enclosure. Table 14 provides physical characteristics for all generator models.

Table 14. Generator Physical Characteristics

Measurements (Typical) - All dimensions nominal	
Lead receptacle(s)	0.126 in (3.2 mm) (single-pin lead)
Dimensions	1.8 in x 1.3 in x 0.27 in (45 mm x 32 mm x 6.9 mm)
Weight	0.56 oz (16 g)
Connector Retention Strength	
With VNS Therapy lead	> 10 N
Package Contents	
	Generator Hex Screwdriver

3.1.2 Biological Compatibility

Materials exposed to the subcutaneous environment are biologically compatible. All of these materials have a long history in medical implants and have been found to be tissue compatible. Table 15 provides a list of component materials for all generator models.

Table 15. Generator Component Materials

Component	Material
Case	Titanium, hermetically sealed
Header	Polyurethane — Tecothane™ TT-1075D-M Thermoplastic
Lead connector blocks	Stainless steel
Setscrew plug	Silicone*

* No component of the VNS Therapy System is made with natural rubber latex.

3.1.3 Power Source

The power source is a Wilson Greatbatch Ltd, lithium carbon monofluoride battery. Table 16 contains battery characteristics.

Table 16. Battery Characteristics

Battery Manufacturer & Model	Battery Chemistry	Open Circuit Voltage	Maximum Capacity	Self Discharge	Voltage Drop at End of Life (EOL)
Wilson Greatbatch Ltd., Model 2183	Lithium carbon monofluoride	3.3 V, open circuit	1 Amp-hour	reduces capacity by <1% per year	gradual drop in voltage at EOL

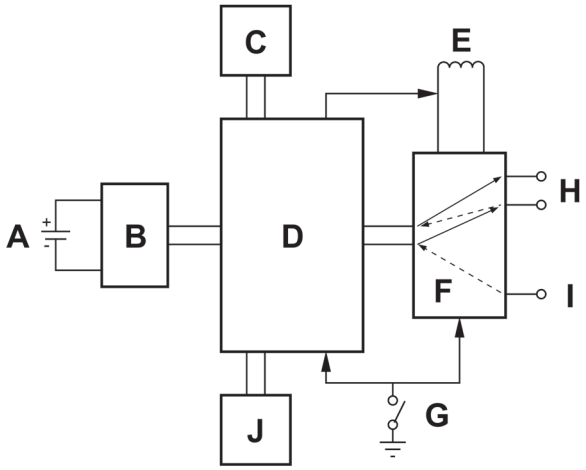
3.1.4 Circuitry

The generator uses complementary metal oxide semiconductor (CMOS) integrated circuits, including a microprocessor. The circuitry is functionally represented in Figure 6.

For descriptive purposes, circuitry of the generator can be divided into the following major functional sections:

Voltage regulators	Regulates the system power supplies
Crystal oscillator	Provides a timing reference
Logic and control	Controls overall generator function; receives and implements programming commands; collects and stores telemetry information, processes sensory input, and controls scheduled and sensory-based therapy outputs
Antenna	Receives programming signals; transmits telemetry information to the programming wand
Reed switch	Provides a mechanism to place the generator in Magnet Mode or to inhibit its output
Input/Output	Develops and modulates signals delivered to the lead; provides amplification of cardiac signals ; allows the traditional VNS electrodes to serve as both therapy outputs and sensing input connections
Accelerometer	Provides information related to patient posture

Figure 6. Generator Circuitry



A Battery

B Voltage Regulator

C Crystal Oscillator

D Logic and Control

E Antenna

F Input/Output

G Reed Switch

H Lead Electrodes

I Titanium Can Connection

J Accelerometer

3.1.5 Identification

The generator can be identified on an x-ray by the x-ray tag codes provided in Table 17. The serial number and model number of the generator are marked on its titanium case, but do not appear on the x-ray.

The serial number and model number are identified by interrogating the generator with the programming system.

Table 17. X-Ray Tag Codes and Further Identification by Serial Number

Model	Possible X-Ray Tag Codes	Further Identification by Serial Number
Model 1000	LIVN and VNS	N/A

Note: See the programming system physician's manuals for details.

3.1.6 Heartbeat Detection Performance

Model 1000 has a heartbeat detection sensitivity of 98% and Positive Predictive Value (PPV) of 98%. Improper implant location and/or inadequate heartbeat detection configuration could negatively impact R-wave detection performance results. See the *Implantation Procedure* for instruction on how to determine implant location and configure heartbeat detection.

3.2 VNS Therapy System Feature Overview and Compatibility

Table 18 provides a high level description of features and compatibility for the Model 1000, including surgical accessories and programming systems.

Table 18. VNS Therapy System Compatibility and Programming Features

Generator	Compatible Lead (Header)	Surgical Accessories	Programming Features	Programming Wand	Programmer
Model 1000	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode Magnet Mode AutoStim Mode Guided Programming Low Heart Rate/Prone Scheduled Programming Day-Night Programming	Model 2000	Model 3000 all versions

Note: A full description of the programming features in Table 18 can be found in "Features and Modes" section of this chapter.

3.3 Directions for Use

3.3.1 Stimulation Parameters

Generator stimulation parameters and available parameter setting are presented in Table 19.

Table 19. Stimulation Parameters & Available Parameter Settings

Stimulation Parameters	Available Parameter Setting
Output current	0-2.0 mA in 0.125-mA steps (± 0.1 mA or ± 10%; whichever is greater) 2-3.5 mA in 0.25-mA steps (± 0.1 mA or ± 10%; whichever is greater)
Signal frequency	1, 2, 5, 10, 15, 20, 25, 30 Hz ±6%
Pulse width	130, 250, 500, 750, 1000 µsec ±10%
Signal ON time	Normal Mode—7, 14, 21, 30, 60 sec AutoStim Mode—30, 60 sec Magnet Mode—7, 14, 21, 30, 60 sec
Signal OFF time	0.2, 0.3, 0.5, 0.8, 1.1, 1.8, 3 min, and 5 to 180 min (5 to 60 in 5-min steps; 60 to 180 in 30-min steps) ± 4.4 sec or ± 1%, whichever is greater
Magnet activation	Provided by magnet application (output current, pulse width, and signal ON time may be independently programmed for this purpose)
Reset parameters	Settings are unchanged, but output is disabled (no stimulation)
Detection Configuration Parameters	
Tachycardia Detection	ON or OFF; allows VNS to operate in standard mode (i.e. no Tachy- Enabled or Disabled; When enabled, allows the device to perform heartbeat sensing and tachycardia detections - "OFF setting) or combination of standard VNS form heartbeat sensing and tachycardia detections with detection (i.e. Tachycardia Detection - "ON" setting).
AutoStim Threshold	Threshold for heart rate increase which triggers Automatic Stimulation (AutoStim). Setting range is from 20% to 70%. 20% is most sensitive. 70% is least sensitive.
Heartbeat Detection Setting (Sensitivity)	Sensitivity parameter for heartbeat detection, ranging from 1 to 5, with "1" being the least sensitive and "5" being the most sensitive setting. **Note**: Model 1000 is capable of detecting heart beats in the range between 28 and 180 bpm (± 10% or 5 bpm, whichever is greater)
Verify Heartbeat Detection	Feature on the programming software that when activated, configures the generator to emit a pulse signal when a heartbeat is detected (for 2 minutes). May be used to check heartbeat detection performance at the currently programmed Heartbeat Detection setting.
Low Heart Rate Threshold	Threshold for low heart rate that triggers logging of the event if it occurs after AutoStim or Magnet Mode stimulation. Available selections include OFF, 30, 40, 50, and 60 bpm. **Note**: "OFF" turns off detection for low heart rate events.
Prone Position Detection	ON or OFF; When ON, configures the Model 1000 to perform detection for prone posture events after an AutoStim or Magnet Mode stimulation

Stimulation Parameters	Available Parameter Setting
Day-Night Programming	
Day-Night Programming	Enabled or Disabled; When enabled, allows user to program the generator to deliver 2 independent sets of stimulation parameters at different times during a 24-hour period.
Nighttime Period	Time period for which Nighttime Values are active; 1-23 hours in 30 minute increments
Nighttime Values	Programmable parameters for Nighttime stimulation includes: ■ Normal Mode, AutoStim Mode, and Magnet Mode output current ■ Normal Mode frequency ■ Normal Mode, AutoStim Mode, and Magnet Mode pulse width ■ Normal Mode, AutoStim Mode and Magnet Mode ON time ■ Normal Mode OFF time ■ Night Time AutoStim threshold AutoStim and Magnet frequency in the nighttime will default to the same value as the Nighttime Normal Mode frequency.
Scheduled Programming Parameters	
Scheduled Programming	Enabled or Disabled When enabled, allows user to schedule automated increases in output current using a protocol of up to 7 steps
Interval Between Steps	Default value: 14 days; range is from 7 days to 28 days
Step Values	Programmable parameters for each step of a protocol: First step: All stimulation parameters Subsequent steps: output currents only
Device History and Diagnostics	
Device History	Patient ID, implant date, model number, serial number, magnet activations, total ON time, total operating time, and manufacturing date. Device settings and stimulation statistics for last 3 office visits. Reference programming system physician's manual for details.
Device Diagnostics	Patient ID, model ID, serial number, firmware build number, implant date, communication status, output current status, measured current delivered, lead impedance, and battery status indicators (IFI, N EOS, EOS) Reference programming system physician's manual for details.

3.3.2 Communicating with the VNS Therapy System

3.3.2.1 Programming system

A compatible VNS Therapy programming system is required to communicate with and program the generator. A programming system consists of a programming wand, and a compatible computer running the programming software.

Note: For more information such as the proper placement of the wand, connection of the wand to the computer, and use of the programming system, see the programming system physician's manuals.

3.3.2.2 Communication

The generator "listens" for a communication signal from the programming wand. Communication usually initiates between 1 and 4 seconds, but may be prolonged or interrupted in the presence of electromagnetic interference (EMI). Depending on the type and amount of information being transferred between the generator and the programming wand, complete communication may take up to one minute. Downloading additional information may take more time.

The generator listens for and implements interrogations, parameter programming instructions, requests for diagnostics testing, and device history inquiries. In response, the generator transmits information on the stimulation parameter settings, changes its parameter settings, responds to requests for diagnostics testing, and provides device histories, respectively. Each time these data are transmitted by the generator, they are saved by the programming software to a database.

Note: For details on viewing generator information on a programming computer, see the programming system physician's manuals.

In addition to the programming system, a magnet can be used for one-way communication to the generator by activating a reed switch in the electronic circuitry. The magnet can be used to initiate stimulation, temporarily inhibit stimulation, perform Magnet Mode diagnostics, or reset the generator.

3.3.3 Features and Modes

3.3.3.1 Normal Mode

After the generator has been programmed, stimulation will repeat in accordance with the programmed ON and OFF cycle (Normal Mode) until the generator receives communication from the programming system, is inhibited with the magnet, or is activated by the magnet, or an AutoStim occurs. Immediately after successful programming, the generator delivers a programmed stimulation that enables the programmer to evaluate patient response. If programming is performed during stimulation, stimulation will be terminated; after programming, stimulation will begin using the revised settings.

3.3.3.2 Magnet Mode

Magnet Mode produces on-demand stimulation for the programmed magnet ON time. Stimulation is initiated by applying or passing the magnet over the generator for 1-2 seconds and then immediately removing it from the area over the generator. Magnet Mode stimulation is delivered after the magnet is removed. The Magnet Mode uses the same frequency as the Normal Mode, but the output current, pulse width, and signal ON time are independently programmable.

The magnet may also be used to inhibit stimulation. To do so, simply place the magnet over the generator and keep in place. The generator will not stimulate until the magnet is removed.

3.3.3.3 AutoStim Mode

AutoStim Mode is an optional feature that monitors heart rates during stimulation OFF times and detects rapid, relative heart rate increases (≥ 20%) that may be associated with seizures. Following detection, on-demand stimulation is delivered.

If AutoStim is enabled, stimulation is initiated automatically upon detection of heart rate rises that exceed the selected threshold for AutoStim. Due to varying physiological conditions among patients, the AutoStim feature has been designed such that the sensitivity of the detection is adjustable for relative heart rate changes of 20% to 70%.

Tachycardia Detection used for the AutoStim feature requires that the generator is accurately measuring heart rate. Therefore, its heartbeat detection accuracy should be verified by the physician at implant and at each office visit. If heartbeat detection is inaccurate, adjustments of the Heartbeat Detection setting may be needed. See "Troubleshooting" in the programming system physician's manuals for more information.

3.3.3.3.1. Tachycardia Detection Algorithm Performance —ROC Curves

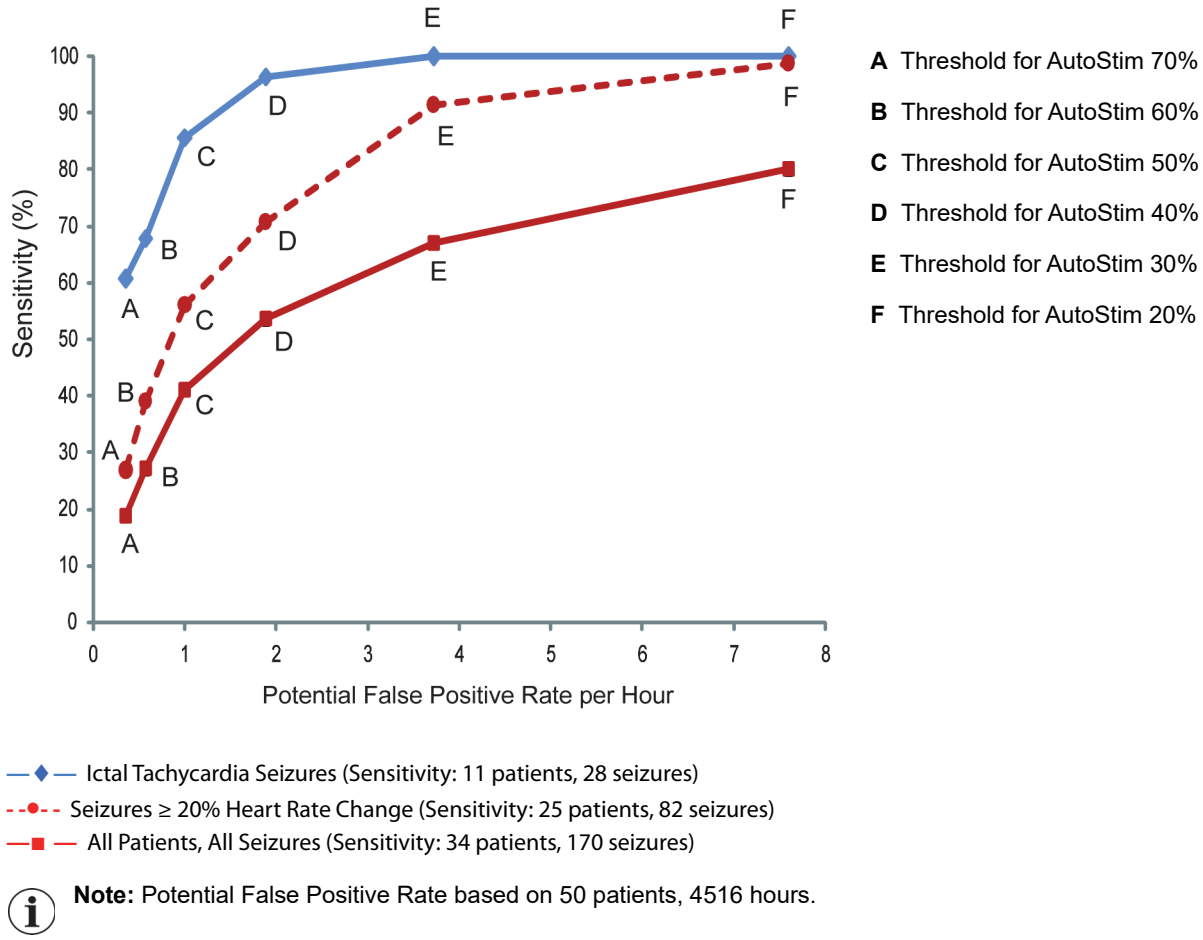
Note: The Tachycardia Detection Algorithm in Model 1000 was tested *in silico* and determined to be functionally equivalent to Model 106. Therefore, no new clinical evaluation for algorithm performance was conducted for Model 1000 and the Model 106 results are applicable.

See Figure 7 for Receiver Operating Characteristic (ROC) Curves using data collected in an EMU setting from two clinical studies (E36 and E37). Curve 1 (blue) includes only seizures that met the criteria for Ictal Tachycardia (defined as an increase in heart rate during a seizure to a rate that was greater than 100 bpm and was at least a 55% increase or 35 bpm increase from baseline [resting] heart rate). Curve 2 (dashed red) includes all seizures with greater than 20% increase in heart rate during an ictal event, and represents the performance for all seizures which may be detected based on the design of the Tachycardia Detection Algorithm. Curve 3 (solid red) includes all seizures from all study patients, irrespective of the heart rate change.The curves illustrate a trade-off between sensitivity and specificity (potential false positive rate per hour) as the AutoStim Threshold setting is adjusted. As one decreases the AutoStim threshold, the sensitivity increases, but at the expense of specificity.

The following limitations should be considered when interpreting the data in Figure 7, as an EMU may not be reflective of real world use:

- The EMU represents a controlled setting and thus, the types of seizures and number of seizures associated with tachycardia may vary from those in real world use.
- During the EMU only the AutoStim feature was enabled and the Normal Mode was disabled. Use of AutoStim in conjunction with Normal Mode stimulation and Magnet Mode stimulation may affect tachycardia detections.
- In real world use, physical activities that increase heart rate, including but not limited to exercise, could result in detection of tachycardia that may not be associated with a seizure.

Figure 7. Receiver Operating Characteristic (ROC) Curve for Tachycardia Detection Associated with Seizures



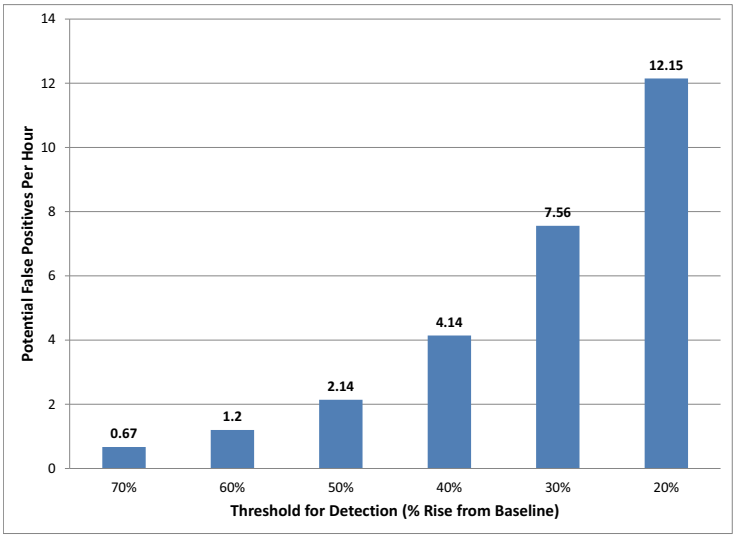
Note: Potential False Positive Rate based on 50 patients, 4516 hours.

3.3.3.3.2. Tachycardia Detection Algorithm Performance —AutoStim Potential False Positives

Note: The Tachycardia Detection Algorithm in Model 1000 was tested *in silico* and determined to be functionally equivalent to Model 106. Therefore, no new clinical evaluation for algorithm performance was conducted for Model 1000 and the Model 106 results are applicable.

ECG data were collected in a previously conducted clinical study of healthy normal volunteers (E-34) during sub-maximal exercise testing and sleep. Figure 8 shows the impact of exercise (i.e. stair stepping and moderate treadmill) and other activities (i.e. Valsalva maneuvers and sleep) on the AutoStim Potential False Positive rate.

Figure 8. Non-Seizure Heart Rate Challenges



Note: In Figure 8, N=49 patients

3.3.3.4 Low heart rate and prone position detection

Caution: Low heart rate and prone position events are for informational purposes only. Detected events are not to be used for alarms or medical diagnosis.

Clinical data suggest that events of cardiac arrest and/or respiratory arrest, possibly aggravated by the prone position, are precursors to instances of Sudden Unexpected Death in Epilepsy (SUDEP)[1]. The generator can detect and log low heart rate and prone position events if they are of interest to the physician. These events are detected after AutoStim or Magnet Mode stimulations, and Tachycardia Detection must be enabled in order to log low heart rate and prone position events.

Detection for low heart rate and prone position events are independently configurable. For use of low heart rate detection, the physician must define a detection threshold, specific for the patient, from 30 to 60 bpm in 10 bpm increments. For prone position detection, a calibration with the patient in supine and upright positions is required prior to the feature activation. Detected events are stored within the generator's memory and viewable during patient follow-up visits through the programmer.

Note: For additional information on use of the feature, refer to the programming system physician's manuals.

[1] Ryvlin, Philippe et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. The Lancet Neurology, Volume 12 , Issue 10 , 966 - 977

3.3.3.5 Scheduled Programming

Caution: This feature may not be appropriate for use in patients who are nonverbal or are unable to use the patient magnet to stop undesired stimulation. Similarly, exercise caution for use of this feature in patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.

Scheduled Programming is an optional feature that allows the physician to program the generator so that it automatically increases stimulation therapy parameters while the patient is in the comfort of his or her home. This feature is intended to be used during the titration phase and could potentially lessen the number of office visits the patient will need to travel to and from the clinic for programming increases only. Physicians have the option of creating a custom programming schedule, or selecting and confirming the use of a standard schedule. The programming schedule is limited to a maximum of 7 steps and the physician specifies the parameter settings for each step as well as the time between steps. Once programmed into the generator, the generator will deliver the stimulation increases for each step at the time(s) and date(s) set by the physician.

If using this feature, it is highly recommended that physicians communicate the date(s) and time(s) of the programming schedule to the patient and/or caregiver so the patient is aware of upcoming parameter increases. If a patient is unable to tolerate a scheduled therapy increase, instruct the patient to disable VNS stimulation with the magnet (i.e. place magnet over the generator) and follow-up with the physician for programming adjustment.

Note: For additional information on use of the feature, refer to the programming system physician's manuals.

3.3.3.6 Day-Night Programming

Caution: Time-based features (e.g., Scheduled Programming, Day-Night Programming) do not automatically adjust for Day Light Savings or time zone changes. Tell the patient to follow-up with the physician for reprogramming if needed.

Day-Night Programming is an optional feature that allows the generator to deliver 2 independent sets of therapy parameters at different times during a 24-hour period. The physician specifies what parameters will change, and a time period during the 24-hours when the alternate parameter set should be active. After the Day-Night program has been defined, the generator will alternate between the 2 independent parameter sets on a daily basis. This feature provides the physician the ability to further customize the delivery of VNS Therapy to accommodate to each individual patient's needs after a target level has been established for the patient.

As with any therapy setting change, the risk and benefits of altering a patient's known efficacious settings should be considered when making adjustments. Inform your patients about when to expect a setting change (i.e. when Daytime settings transition into Nighttime settings). In addition, patient tolerability of the alternate parameter set should be assessed prior to the patient leaving the office visit.

Note: For additional information on use of the feature, refer to the programming system physician's manuals.

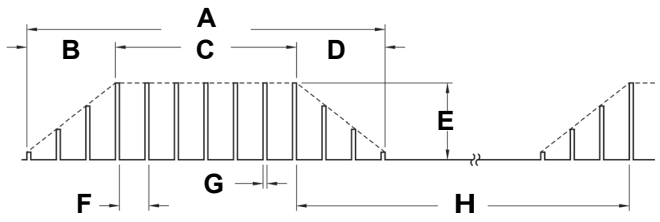
3.3.4 Stimulation Parameters, Duty Cycle, and Impacts on Battery Life

3.3.4.1 Programmable parameters

A graphic representation of stimulation (Figure 9) depicts the relationship of the programmable parameters. Each parameter can be independently programmed, thereby offering multiple setting combinations from which the physician may select optimal stimulation for the patient.

Figure 9 shows that the output pulse can be varied both by amplitude (output current) and duration (pulse width). The number of output pulses delivered per second determines the frequency.

Figure 9. Stimulation



A Stimulation Time

B Ramp Up (2 sec.)

C On Time

D Ramp Down (2 sec.)

E Output Current

F 1/Signal Frequency

G Pulse Width

H Off Time

Note: Frequencies <10 Hz do not ramp

3.3.4.2 Duty cycle

The percentage of time the generator is stimulating is called a “duty cycle.” A duty cycle is calculated by dividing the stimulation time (programmed Normal Mode ON time plus, if frequency is ≥ 10 Hz, 2 seconds of ramp-up time and 2 seconds of ramp-down time) by the sum of the ON and OFF times. The various parameter settings for stimulation are listed in “Stimulation Parameters”.

Warning: Excessive stimulation is the combination of an excess duty cycle (i.e. one that occurs when ON time is greater than OFF time) and high frequency stimulation (i.e. stimulation at ≥ 50 Hz). Excessive stimulation has resulted in degenerative nerve damage in laboratory animals. Furthermore, excess duty cycle can be produced by continuous or frequent magnet activation (> 8 hours). While LivaNova limits the maximum programmable frequency to 30 Hz, it is recommended that you do not stimulate with excess duty cycle. Further, physicians should warn patients about continuous or frequent magnet use as this could lead to early battery depletion.

Table 20 shows duty cycles for typical ON time and OFF time settings.

Table 20. Duty Cycles for Various ON and OFF Time Settings

	OFF Time (min)								
	0.2	0.3	0.5	0.8	1.1	1.8	3	5	10
ON Time (sec)	**Duty Cycles* (% ON Time)**								
7	58	44	30	20	15	10	6	4	2
14	69	56	41	29	23	15	9	6	3
21	76	64	49	36	29	19	12	8	4
30	81	71	57	44	35	25	16	10	5
60	89	82	71	59	51	38	27	18	10

* A duty cycle is calculated by dividing stimulation time (programmed ON time plus 2 seconds of ramp-up time and 2 seconds of ramp-down time) by the sum of the ON time and the OFF time.
The duty cycles in gray are not recommended as they represent parameter combinations with ON Time > OFF Time.

Note: If Tachycardia Detection is enabled and AutoStim output current is > 0 mA, Normal Mode OFF Times < 1.1 minutes are not available for programming.

3.3.4.3 Parameter settings and battery life

When selecting a combination of parameter settings for stimulation, the physician should also consider that some combinations would decrease battery life faster than others. Tachycardia Detection and/or additional features will also decrease the battery life.

Note: See "Generator battery longevity".

Table 21 shows the longevity impact that the AutoStim Mode feature has with a typical lead impedance (3 kOhms) and the following Normal mode settings: 2 mA output current, 20 Hz signal frequency, 250 µsec pulse width , and 10% duty cycle (30 sec ON, 5 min OFF).

Table 21. Estimated Longevity with Sensing and AutoStim

AutoStim Feature	Expected Life (yrs)
Tachycardia Detection / AutoStim "OFF"	11.5

	AutoStim ON-Time	
Tachycardia Detection / AutoStim "ON"	30 sec	60 sec
AutoStims Per Hour	**Expected Life (yrs)**	
1	7.6	7.5
7	7.0	6.1
15	6.4	4.9

3.3.5 VNS Therapy magnets

There are four possible uses of the magnet:

- To provide on-demand stimulation as an attempt to abort or deintensify an oncoming seizure or a seizure in progress. During an aura or at the start of a seizure, magnet activation may be initiated by the patient, a companion, or the physician by applying or passing a magnet over the generator to activate a reed switch in the generator's electronic circuitry. This action changes the generator from Normal Mode or AutoStim to Magnet Mode.
- To temporarily inhibit stimulation
- To reset the generator (in combination with the programming system)
- To test daily the functioning of the generator, LivaNova recommends that patients be instructed to use the magnet to activate stimulation. Note that this indirectly tests the generator through the ability of the patient to perceive Magnet Mode stimulation. Since patients may become accustomed to their stimulation settings over time, it is recommended that physicians always use the Diagnostics testing available in the programming software in order to formally test the implanted system.

Warning: Excessive stimulation is the combination of an excess duty cycle (i.e. one that occurs when ON time is greater than OFF time) and high frequency stimulation (i.e. stimulation at ≥ 50 Hz). Excessive stimulation has resulted in degenerative nerve damage in laboratory animals. Furthermore, excess duty cycle can be produced by continuous or frequent magnet activation (>8 hours). While LivaNova limits the maximum programmable frequency to 30 Hz, it is recommended that you do not stimulate with excess duty cycle. Further, physicians should warn patients about continuous or frequent magnet use as this could lead to early battery depletion.

3.3.5.1 Magnet activation technique

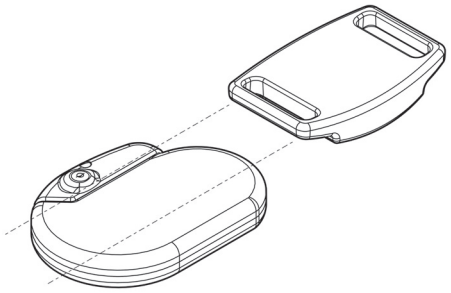
To initiate stimulation, apply or pass the magnet over the generator for 1-2 seconds and then immediately remove it from the area over the generator. The proper orientation and motion for initiating magnet activation is shown in Figure 10. An optional cross-pattern swipe, also shown in Figure 10, may be used by the patient or caregiver to activate the Magnet Mode if difficulty is encountered with a single pass of the magnet. Removal of the magnet causes the generator to operate in Magnet Mode, delivering a single stimulation at the programmed magnet pulse width, magnet current, and magnet signal ON time settings. The frequency is the programmed value for Normal Mode. A Magnet Mode stimulation will always override any Normal Mode programmed stimulation. If Magnet Mode stimulation is not desired, the Magnet Mode output current may be programmed to 0 mA.

Caution: The cross-pattern swipe technique may cause duplicate magnet activation entries to be shown in the programming software database. This is an expected occurrence due to device design and is not considered a device malfunction.

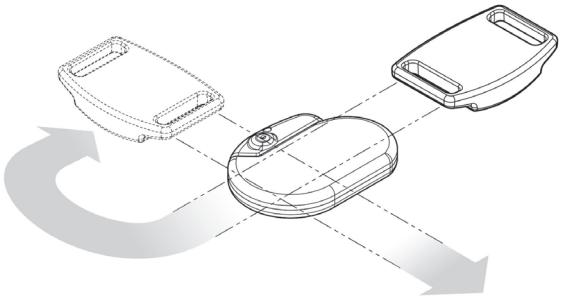
It is recommended that tests of the magnet output be performed while the patient is still in the physician's office to ensure tolerability of the magnet output.

Figure 10. Initiate Magnet Activation

Standard Magnet Activation



Optional Cross-Pattern Magnet Activation



Caution: To activate or stop stimulation, the label side of the magnet should face the generator.

3.3.5.2 Inhibit generator output with the magnet

Application of the magnet during stimulation will inhibit the output. In addition, holding the magnet in place will terminate any ongoing Normal or AutoStim Mode stimulation. Table 22 provides the amount of time the magnet should be held in place to terminate Normal or AutoStim Mode stimulation for each generator model. After the magnet is removed, Normal Mode operation will resume with stimulation when one complete OFF time has elapsed.

Table 22. Amount of Time Magnet is Held in Place to Terminate Normal or AutoStim Mode Stimulation

Generator	Amount of Time
Model 1000	10 sec.

Caution: If stimulation becomes painful, the patient should be instructed to stop the stimulation with the magnet.

In the unlikely event of continuous stimulation or other malfunction, the patient must be advised to apply the magnet, secure it in place, and immediately notify their physician.

Note: See "Adverse Events" in the *Epilepsy Information-Clinical Studies* chapter.

3.3.5.3 Reset the microprocessor with the magnet and the programming system

The VNS Therapy System allows the generator microprocessor to be reset in the event of a malfunction. Resetting is necessary only in the rare case of microprocessor memory malfunction, which might be caused by conditions described in the *Introduction to the VNS Therapy System* chapter. Resetting the microprocessor may be appropriate when the generator and the programming system are unable to communicate.

Caution: *Generator reset*— When a generator is reset, optional features (such as Day-Night Programming) and stimulation output are disabled (0 mA); however, all settings and device history are preserved. After a successful reset, the generator stimulation output may be re-enabled to resume operation at the previously programmed settings and optional features reactivated.

For suggestions in solving communication difficulties, see "Troubleshooting" in the programming system physician's manuals.

For instructions on how to reset the microprocessor, see the programming system physician's manual. It is recommended, except in cases of a medical emergency, that the physician consult a LivaNova technical representative before a reset is performed.

3.3.6 Device History

The generator device history consists of generator serial number, model number, patient code, implantation date, and other information pertinent to diagnostic and programming events. Use the programming system to access and view generator device history information.

3.3.7 Device Diagnostics

Information from device diagnostic tests can help the physician determine whether the:

- Generator output current is being delivered at the programmed value
- Lead impedance is within an acceptable range
- Generator battery is at a sufficient level

Note: For details on available diagnostic tests, see the programming system physician's manuals.

3.3.7.1 System Diagnostics test

The System Diagnostics evaluates the lead impedance of the VNS Therapy System, as well as the generator's ability to deliver the programmed Normal Mode stimulation. Depending on the generator model and programmed Normal Mode output current, different test pulses may be conducted during the test (see Table 23). The programming software will report the lead impedance and whether the programmed stimulus was delivered.

Table 23. System Diagnostics

Normal Mode Output Current	System Diagnostics Behavior
0 mA	Delivery of programmed output for approximately 4 seconds, followed by one brief pulse at 0.25 mA for less than 130 µsec.*
>0 mA	

*Minor differences in the system diagnostics test exist for M1000 with serial numbers <100,000. Refer to the *Introduction to the VNS Therapy System* chapter for more information.

Note: Once programmed ON, lead impedance measurement readings are automatically performed once every 24 hours.

3.3.7.2 Reasons for high or low lead impedance readings

Possible causes of high lead impedance readings are thought to include:

- Lead discontinuity
- Lead disconnection from the generator
- Fibrosis between the nerve and the electrode
- Electrode detachment from the nerve
- Defective generator

Possible causes of low lead impedance readings are thought to include:

- Short-circuit condition within the lead
- Defective generator

3.3.7.3 High lead impedance: possible implications

High lead impedance (≥ 5300 Ohms), in the absence of other device-related complications, is not an indication of a lead or generator malfunction. High lead impedance in combination with the patient's failure to feel even the maximum output stimulus may indicate a lead wire fracture or other type of electrical discontinuity in the lead. Complications with heartbeat sensing may also be indicative of a lead discontinuity. Patients experiencing high lead impedance, no sensation of maximum output stimulation, and an increase in seizures symptoms should be further evaluated for possible lead replacement.

Note: For additional instructions on how to perform the System Diagnostics, see the programming system physician's manuals.

Note: To troubleshoot high or low impedance see "Troubleshooting" in the programming system physician's manuals.

3.3.7.4 Low lead Impedance: possible implications

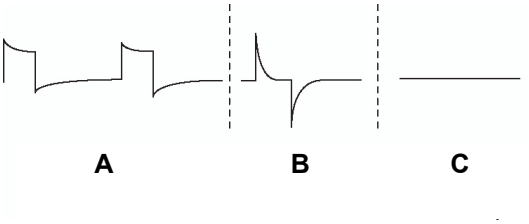
Low lead impedance (≤ 600 Ohms) likely indicates the existence of a short-circuit condition, although an impedance value of greater than 600 Ohms does not exclude the possibility. A sudden decrease in impedance value in combination with device-related complications (e.g., increase in seizures symptoms or painful stimulation; patient perception of feeling erratic,

limited, no stimulation, or complications detecting heartbeats) may also indicate a short-circuit condition in the lead.

3.3.7.5 Stimulus waveform analysis

Either evoked potential monitoring equipment or an oscilloscope can be used to analyze the stimulus waveform from the neck for verification of an electrical discontinuity. A differentiated waveform with narrowed pulses or no waveform at all can confirm a discontinuity. Figure 11 shows characteristic waveforms obtained from skin electrodes for a lead that is intact and for a lead that has a fracture in one or both wires. In addition, lead discontinuities can sometimes be identified on an x-ray of the implant site.

Figure 11. Typical Waveforms Obtained from Skin Electrodes



A Intact Lead

B One Broken Lead Wire

C Two Broken Lead Wires or No Output

3.3.8 Delivery of programmed output current

3.3.8.1 LOW as output current

If the diagnostic tests indicates LOW output current, the generator may not be delivering the programmed output current. Reasons for failure to deliver the programmed output current include high programmed output current and high lead impedance. The maximum deliverable output current, according to Ohm's Law, equals the maximum output voltage (approximately 12 V) divided by the lead impedance.

3.3.8.2 Reprogram to a lower current

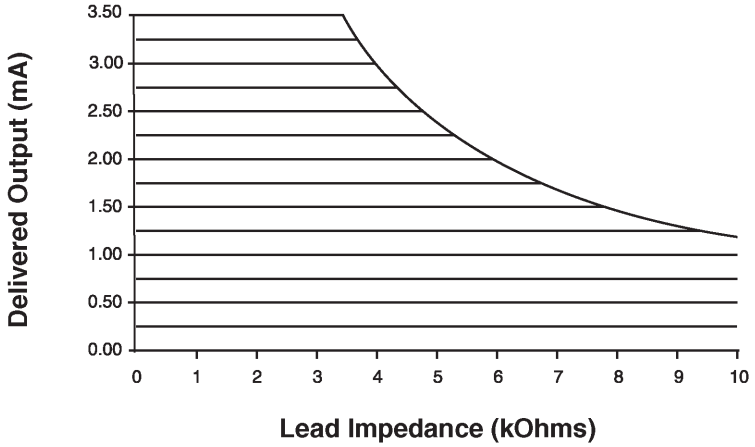
If the generator is failing to deliver the programmed output current, the physician can reprogram the device to a lower output current and attempt to compensate for the decrease in delivered energy by widening the pulse width. For example, if the diagnostics read LOW or LIMIT for a generator programmed at 2.5 mA, 30 Hz, 500 µsec with 30 seconds ON time, then the parameters may be changed by lowering the output current to 2 mA and widening the pulse width to 750 µsec.

3.3.9 Charge delivered per pulse

Output current x pulse width = charge delivered per pulse

The charge delivered per pulse is the most important parameter in evaluating stimulation output. It is defined as a microcoulomb (µC), which is the product of current and time—that is, the output current (mA) multiplied by the pulse width (µsec). Figure 12 shows the relationship of delivered output current (mA) to lead impedance for a 1000 µsec pulse with output currents from 0 to 3.5 mA.

Figure 12. Relationship of Delivered Output Current to Lead Impedance



3.3.10 Generator battery longevity

3.3.10.1 Battery longevity and programmed setting choices

The anticipated longevity of the generator battery varies, depending on the choice of programmed settings. Higher output currents, frequencies, pulse widths, and duty cycles generally deplete the battery over a shorter period of time than lower settings. Generally, the increase in battery depletion rate is proportional to the increase in the programmed setting in the absence of detection.

⚠ **Caution:** *Undeliverable output currents*— Programming the generator to a high output current that cannot be delivered due to a high lead impedance may disproportionately increase the battery depletion rate and should be avoided.

Other factors, such as lead impedance, magnet usage or use of optional features (e.g., AutoStim Threshold settings, AutoStim) also affect the anticipated battery longevity. The anticipated battery longevity decreases as lead impedance increases. Although 1.5 k to 3 kOhms may be a typical lead impedance at implantation, the impedance may increase to 3 k to 5 kOhms during the life of the implant.

The *Appendices* chapter provides estimated battery lifetimes under a variety of stimulation conditions. Because of the number of possible parameter combinations, it is impractical to provide the projected life for all possible combinations. The tables should not be used to predict battery end of service (EOS), but they give some indication of the effect of various parameter changes on battery life and can be used to assist in the selection of parameter settings. They also indicate that battery life can be maximized at low duty cycles and low frequencies (e.g., 20 Hz) for stimulation.

ⓘ **Note**: For more information, see the programming system physician's manuals.

3.3.10.2 Battery status indicators

The programming software displays a battery indicator similar to an indicator that may be found in cell phones. The visual indicator illustrates the approximate remaining battery capacity.

The programming software will display warning messages after an interrogation or programming of the generator if the battery has been depleted to a level where action is recommended due to approaching or reaching End of Service (EOS). Please refer to the programming system physician's manuals for additional information on these indicators.

Caution: *Battery evaluation at cold temperatures*—Low storage temperatures may affect the battery status indicators. In such cases, the battery status indicators should be re-evaluated using the System Diagnostics or Generator Diagnostics after the generator has been at room or body temperature for 30 minutes.

3.3.11 Generator Replacement

All VNS Therapy generators eventually require surgical replacement as a result of battery depletion. Generator replacement does not, of itself, require lead replacement unless a lead discontinuity is suspected. Generator replacement or removal requires dissection to the generator's pocket, with care being taken not to damage or cut the lead. The entire surgical procedure generally requires about 1 hour.

3.3.11.1 Signs of End of Service

The most common reason for the absence of stimulation is battery depletion, although there may be other reasons. When end of service (EOS) occurs, the generator will disable stimulation and no output will be delivered. If the generator is not explanted or replaced at EOS, the battery voltage will continue to gradually decrease and communication with the generator may not be possible.

Caution: Generator EOS may result in increased frequency, intensity, or duration of signs and symptoms of the patient's disorder, in some cases to levels greater than those reported before stimulation.

3.3.11.2 Replacement Based on Battery Status Indicators

The generators and the programming system have battery status indicators. These indicators provide warnings that a generator battery should be monitored more frequently, is nearing EOS, or has reached EOS. Once these warning messages appear, see recommendations in the programming system physician's manuals.

Note: See "Battery status indicators".

Caution: *Prompt generator replacement***—**LivaNova recommends prompt replacement of the generator at or before EOS. Prompt replacement may help minimize any possible relapse.

Caution: *Explanted generator*—A generator explanted for any reason should not be reimplanted. An explanted generator should be returned to LivaNova. (For instructions on returning an explanted generator, see the *Introduction to the VNS Therapy System* chapter.)

4 Implantation Procedure

4.1 Physician Training / Information

All programming should be by or under the supervision of a physician familiar with the use and operation of the programming software.

Physicians implanting the VNS Therapy System should be thoroughly familiar with all associated training materials, including:

- Product labeling for the generator, lead, programming system, and accessories (magnet, tunneler, and accessory pack), and patient labeling
- Electrode practice fixture—a device used to practice placing the helices around the left vagus nerve

Note: If further assistance is needed, contact Technical Support.

4.2 VNS Therapy Devices and Surgical Materials

4.2.1 New Implants

For new implants, the following devices are needed for surgery:

- 2 generators (1 primary and 1 back-up)
- 2 leads (1 primary and 1 back-up)

4.2.2 Replacement Implants

For replacement implants, the following devices are needed for surgery:

- 1 replacement generator and/or lead
- At least 1 back-up generator and/or lead

4.2.3 Other LivaNova Products - New and Replacement

- 1 tunneler (sterile)
- 1 accessory pack (sterile), which includes resistors (single and dual pin), and items also found in the generator and lead packages (hex screwdriver, tie-downs)
- 1 programming system (non-sterile)

Note: Remember to use proper technique for introducing non-sterile items into a sterile field.

4.2.4 Surgical Materials

Note: The materials and equipment listed below are not provided by LivaNova.

The following is a list of additional materials typically used during the VNS Therapy implantation procedure:

All Generators

- Sterile Laser Arm Bag or equivalent (required)

- Vessel loops and/or silicone sheet for manipulation of the vagus nerve (suggested but optional)

Generators with AutoStim feature

The following materials are required to identify acceptable implant locations:

- Commercial ECG monitor — The ECG monitor should have the capability to print out the ECG waveform/amplitudes on the lead I channel
- Standard, 10 mm Ag/AgCl skin electrodes
- Commercial ECG Instructions For Use

Note: See "Determine acceptable device implant locations (tachycardia detection only)" for details. This information is also summarized in the *Pre-Surgical Evaluation Tool* in the generator sales pack.

4.2.5 To Open the Sterile Pack

Caution: The sterile lead pack should only be opened after exposing the vagus nerve and selecting the VNS Therapy lead helical that best fits.

Caution: Do not open the sales pack if it has been exposed to extreme temperatures or if there is any indication of external damage or damage to the package seal. Instead, return it unopened to LivaNova.

Before the sterile pack is opened, it should be examined carefully for evidence of damage or compromised sterility. If the outer sales pack or inner sterile pack has been opened or damaged, LivaNova cannot guarantee sterility of the contents, and it should not be used. An opened or damaged product should be returned to LivaNova.

To open the sterile pack, do the following:

1. Grasp the tab, and peel back the outer cover.
2. Observing sterile technique, lift out the sterile inner tray.
3. Grasp the inner tray's tab, and carefully peel off the inner cover to expose the contents without dropping them.

4.3 Recommendations for Implantation

In general, implantation of the VNS Therapy System is similar to accepted practice for implantation of a cardiac pacemaker, with the exception of the placement of the helices and the subcutaneous routing of the lead body. The surgical approach and techniques will vary with the preference of the surgeon. To ensure correct lead placement, this chapter of the physician's manual provides recommendations for implantation, order of placement of the helical electrodes and anchor tether, and other essential steps.

Caution: To maximize system performance and minimize possible mechanical damage to the nerve or lead, **pay careful attention to helical placement and lead routing.**

For generators with the AutoStim feature, the physical location of the device critically affects its ability to properly sense heartbeats. Therefore, care must be taken to follow the implant location selection process outlined in "Determine acceptable device implant locations (tachycardia detection only)".

Note: The implant location selection procedure may be performed pre-operatively as part of the patient's surgical work-up.

Critical to the long-term success of the implant are proper techniques both for the attachment of the electrodes and the anchor tether to the left vagus nerve, and for the provision of adequate strain relief below and above the sternocleidomastoid muscle. For general placement of the generator and lead, see Figure 16.

It is recommended that the lead body be coiled and placed in the chest pocket to the side of the generator.

Adequate exposure of the vagus nerve (> 3 cm) facilitates placement of the helices on the nerve. Stretching the nerve or allowing it to dry during implantation may result in temporary swelling of the nerve. Constriction of the nerve or other nerve damage may result in vocal cord dysfunction.

LivaNova recommends that output of the generator and performance of the implanted system be tested at the time of implantation. Although an oscilloscope can be used for measurements, LivaNova recommends use of the appropriate version of the programming software and wand (placed in a sterile drape) for routine system verification.

After the electrode is placed on the nerve, test the electrode-nerve interface impedance by connecting the lead directly to the generator and performing a System Diagnostics (Lead Test). If required, a separate resistor assembly from the accessory pack can be used while performing the optional Generator Diagnostics (Pre-Implant Test).

Note: See "Test the VNS Therapy System".

4.3.1 Before Surgery and Outside of the Sterile Field

4.3.1.1 Interrogate the device

To ensure proper device communication, interrogate the device while still in the sterile pack. For a detailed explanation, see the programming system physician's manuals.

Caution: (For 103 and subsequent models only) If interrogating a generator that has been exposed to low temperatures within the last 24 hours, low battery status indicator(s) may be displayed. See "Troubleshooting" in the programming system physician's manuals.

4.3.1.2 Program patient data

Program the patient identification and implant date into the generator. For a detailed explanation, see the programming system physician's manuals.

4.3.1.3 Determine acceptable device implant locations (tachycardia detection only)

The implant location of generators capable of tachycardia detection critically affects their ability to properly sense heartbeats. The following steps describe the recommended process in identifying acceptable implant locations for the generator and lead.

Note: The implant location selection process is also summarized in the *Pre-Surgical Evaluation Tool* in the generator sales pack.

4.3.1.3.1. Equipment / Materials Required

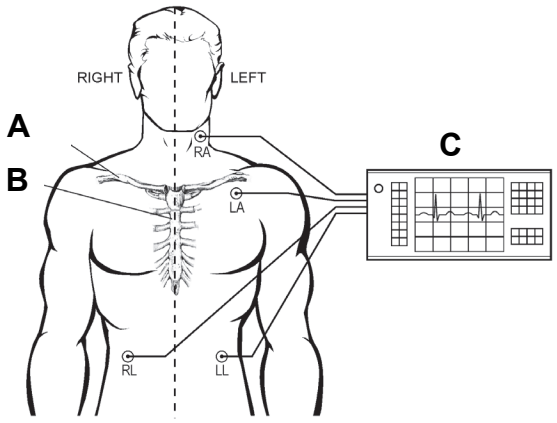
- Commercial ECG monitor
  - The ECG monitor should have the capability to print out the ECG waveform/amplitudes on the lead I channel.
  - The ECG monitor must be configurable to a lowpass filter setting up to 150 Hz.
- Standard, 10 mm Ag/AgCl skin electrodes
- Commercial ECG Instructions For Use

Note: Any commercial ECG system meeting the requirements in the section "Equipment / Materials Required" above is acceptable for use in the identification of potential implant locations procedure. Refer to the commercial ECG system Instructions For Use for proper operation or configuration.

4.3.1.3.2. Procedure

1. Verify that the ECG monitor printing scale is set to 10 mm/mV and the lowpass filter does not exceed 150 Hz.
2. Prepare the patient's skin in the left neck and chest area (e.g. remove excess body hair, perform alcohol wipe) to ensure proper contact with ECG skin electrodes.
3. Place ECG skin electrodes on the patient (a sample configuration is shown in Figure 13) as follows:
   - One electrode should be placed on the left neck, at the approximate intended implant location of the lead electrodes
   - One electrode should be placed on the chest, at the approximate intended implant location of the generator
   - One electrode should be placed on the right lower abdomen or leg
   - One electrode should be placed on the left lower abdomen or leg

Figure 13. Sample Electrode Configuration



A Collar Bone

B Sternum

C ECG Monitor

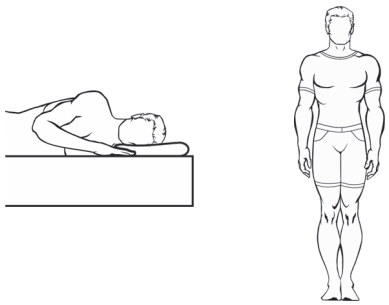
RA Intended implant position of the lead electrodes

LA Intended implant position of the generator

4. Connect the ECG leads to the electrodes:
   - RA - neck
   - LA - chest
   - RL - right lower abdomen or right leg
   - LL - left lower abdomen or left leg
5. Verify that the lead I ECG waveform is showing on the ECG monitor, wait for the ECG signal to stabilize, and collect 10 seconds of ECG data with the patient positioned lying on the left side (first of the two positions in Figure 14).

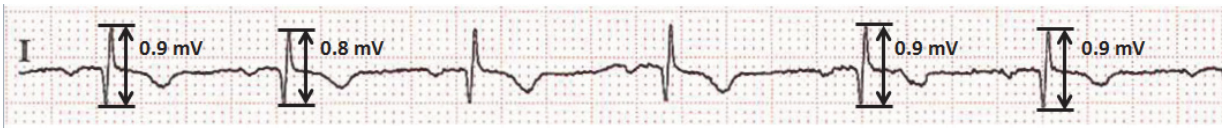
Note: Refer to the commercial ECG Instructions For Use for proper operation or configuration.

Figure 14. Patient Positions



6. Print the ECG strip and label the patient position. On the ECG strip measure the peak-to-peak R-wave amplitude in the lead I channel (see Figure 15) by following the scaling in Step 1. Perform this for at least 4 representative R-waves in the 10 seconds of data and record the minimum amplitude value from the assessed R-waves. This value is representative of the minimum peak-to-peak R-wave amplitude for the patient in the defined body position.

Figure 15. Sample ECG Trace with Peak-to-Peak R-wave Measurements



Note: 1 small division line = 0.1mV, assuming a 10 mm/mV scale.

7. Verify that the minimum peak-to-peak R-wave amplitude measurement in Step 6 is 0.4 mV or greater. If this is the case, then repeat Steps 5-6 with the remaining body position defined in Figure 14 (e.g., standing with arms at side) until both body positions have been tested and the minimum peak-to-peak R-wave amplitude measurement for each body position is confirmed to be 0.4 mV or greater.

   Note: Assuming a 10 mm/mV scale, the peak-to-peak R-wave amplitude measurements must span at least 4 lines on the ECG paper to meet the minimum requirement of 0.4 mV.

8. If the minimum peak-to-peak R-wave amplitude measurement for any one position is less than 0.4 mV, pick a new potential implant location for the generator which increases the distance between the neck electrode and the existing chest electrode, and/or is closer to the patient's heart. Place a new electrode on the new potential implant location (the old chest electrode may be removed if it is in the way), connect it to the LA lead, and repeat Steps 5-7 for both body positions until a location with adequate peak-to-peak R-wave amplitude can be identified.

   Note: Try to place the generator at rib 4 or above, so the patient can have the maximum flexibility for MRI post-operatively. See *MRI with the VNS Therapy System* instructions for use for details.

9. When both body positions have been tested and the minimum peak-to-peak R-wave amplitude measurement for each body position is confirmed to be 0.4 mV or greater, the neck and chest electrode locations are acceptable selections for the implant. Mark the spots on the neck and chest where the electrodes are and use these locations as the intended implant location during surgery. The minimum peak-to-peak R-wave amplitude measurements from the different body positions are used to configure heartbeat detection and tachycardia detection (see "Heartbeat Detection and Tachycardia Detection Configuration") and post operatively to optimize the heartbeat detection setting (see "Optimize the Heartbeat Detection Setting" in the *Epilepsy Information—Patient Follow Up* chapter).

If all practical implant locations have been exhausted without identifying a location which yields a peak-to-peak R-wave amplitude of at least 0.4 mV at both body positions, the AutoStim Mode feature is not suitable for the patient.

4.3.2 Implantation Procedure Overview

Caution: This procedural overview is not a substitute for the complete implantation procedure. See detailed steps that follow.

Note: For generators capable of tachycardia detection, try to implant the lead and generator in the same approximate positions as determined in "Determine acceptable device implant locations (tachycardia detection only)".

The following overview summarizes the implantation procedure:

1. Expose the left carotid sheath and left vagus nerve.
2. Create a pocket in the chest for the generator.
3. Choose the correct size lead.
4. Tunnel the lead subcutaneously from the neck to the generator pocket in the chest.
5. Attach the electrodes and anchor tether to the left vagus nerve.
6. Secure the lead parallel to the nerve.
7. Form the strain relief bend and strain relief loop.

8. Connect the lead to the generator.
9. Verify that the connector pin is fully inserted, and tighten the setscrew.
10. Perform the System Diagnostics (Lead Test).
11. Place the generator in the chest pocket, with the extra coiled lead to the side of the generator, not behind it.
12. **(**For generators capable of tachycardia detection, configure detection settings and verify heartbeat.
13. Secure the generator to fascia; do not place sutures directly around or on the lead.
14. Perform the second System Diagnostics (Lead Test).
15. Interrogate the generator to verify current is 0 mA.
16. Irrigate the incision site with bacitracin or other solution.
17. Close the incisions.

4.3.3 Prepare for Surgery

The surgeon should ensure that the generator, lead, and tunneler are compatible.

LivaNova recommends that the patient be given antibiotics preoperatively and that both incision sites be irrigated frequently with generous amounts of bacitracin or equivalent solution prior to closure. (These incisions should be closed with cosmetic closure techniques to minimize scarring.) Also, antibiotics should be administered postoperatively at the discretion of the physician.

⚠ **Caution**: **Infections related to any implanted device are difficult to treat,** and explantation of the VNS Therapy System may be required.

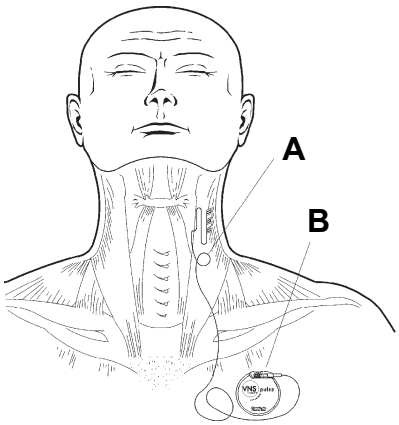
4.4 Lead and Pocket Location

The generator is usually implanted just below the clavicle in a subcutaneous pocket in the left upper chest. Try to place the generator at rib 4 or above, so the patient can have the maximum flexibility for MRI post-operatively. See *MRI with the VNS Therapy System* instructions for use for details.

Suggested placement for the lead is the area of the left vagus nerve half-way between the clavicle and the mastoid process, with the lead subcutaneously tunneled between the incision site in the neck and the pocket formed in the upper chest (see Figure 16). It is recommended that both the lead body and the generator be positioned on the left side of the body. The VNS Therapy tunneler is recommended for subcutaneous routing of the lead.

ⓘ **Note:** For placement of generators capable of tachycardia detection, see “Determine acceptable device implant locations (tachycardia detection only)”.

Figure 16. Placement of Generator and Lead



A VNS Therapy Lead

B VNS Therapy Generator

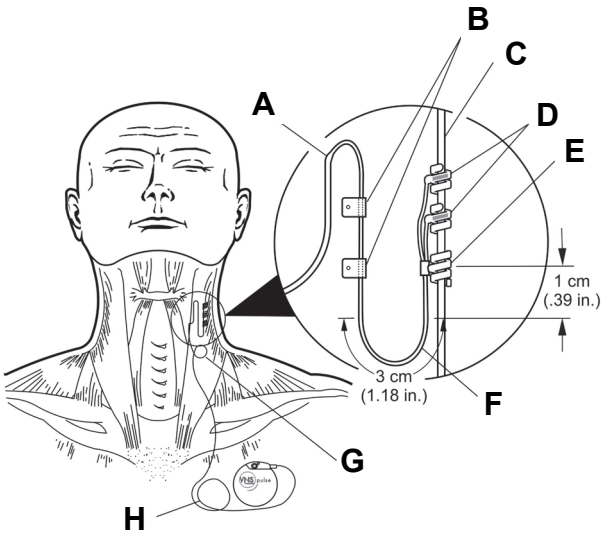
4.5 Begin the Procedure

While the specific surgical approach and techniques for implanting the lead will vary with the implant surgeon, the following detailed instructions are provided for guidance:

1. After administering appropriate anesthesia to the patient, expose the left carotid sheath as it extends along the anterior border of the sternocleidomastoid muscle.
2. Locate and expose *at least 3 centimeters (1.18 inches)* of the left vagus nerve. The recommended stimulation site is a 3-cm section of the vagus nerve, approximately half-way up between the clavicle and the mastoid process, where it is clear of branches (below where the superior and inferior cervical cardiac branches separate from the vagus nerve—see Figure 17 and Figure 19). The nerve usually lies in a posterior groove between the carotid artery and internal jugular vein.

Caution: Avoid letting the vagus nerve become dry during surgery, because dehydration of the nerve can result in nerve damage and swelling.

Figure 17. Electrode Placement



A Lead

B Tie-Downs

C Vagus Nerve

D Helical Electrodes

E Anchor Tether

F Strain Relief Bend

G Strain Relief Loop

H Coiled Extra Lead

3. Create a subcutaneous pocket in the chest below the clavicle for the generator. The pocket depth should not be deeper than 1 inch beneath the skin. It is not recommended to implant the generator below muscle. Doing so may contribute to communication difficulties once implanted.

Note: It is preferable to place the subcutaneous pocket along the axillary border, at or above rib 4.

4.6 Implant the Lead

To implant the lead, follow these steps:

4.6.1 Choose a Lead

1. Choose the appropriately sized lead (2.0 or 3.0 mm electrode inner diameter) carefully. It should fit snugly without constricting the nerve. The lead (2.0 mm/0.08 in) should accommodate most nerves.

Note: For lead size availability, see "Product Specifications" in the lead-specific Technical Information chapters.

Caution: The lead is available in multiple sizes. Since it is not possible to predict in patients what size lead will be needed, **It is recommended that at least one alternate lead size be available in the operating room.** In addition, backups for leads should be available in the event of compromised sterility or damage induced during surgery.

Caution: Do not expose the lead to dust or other similar particulates, because its silicone insulation can attract particulate matter.

Caution: Do not soak the lead in saline or similar solution before implanting it, because this may cause the insulated portions of the connector pin to swell and become difficult to insert into the generator.

4.6.2 Pass the Tunneler and Lead

The tunneler is used to tunnel the lead connector and lead body subcutaneously between the neck incision site and the generator in the chest pocket.

Note: A detailed description of the tunneling tool can be found in the *Tunneler Directions for Use.*

Caution: To maximize system performance and minimize possible mechanical damage to the nerve or lead, pay careful attention to lead routing, lead stabilization, and electrode placement.

Caution: Never route the lead through muscle.

Caution: Never suture the lead or lead body to muscle tissue.

Caution: Always use the tie-downs.

Caution: Do not place sutures directly on the lead body. Doing so may result in insulation damage or wire failure, causing premature failure of the lead.

If necessary, the tunneler can be manually shaped to help direct it through the body.

Caution: Do not manually shape the tunneler **more than 25 degrees** because doing so may cause the sleeve to bend or kink.

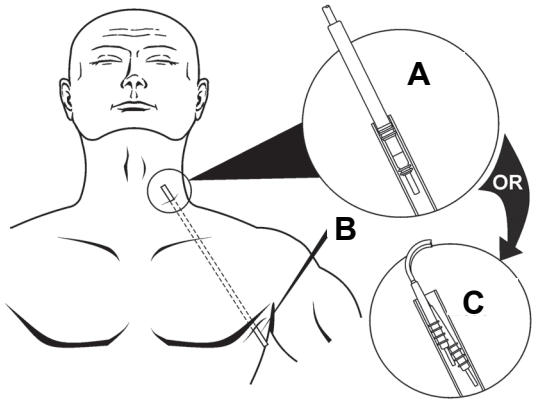
To pass the tunneler, do the following:

1. Place the bullet-tip end of the tunneler through the neck incision and tunnel subcutaneously toward the chest incision, exerting force on the handle end and directing the tunneler as necessary.

   As an alternative, the lead connector and lead body can be tunneled subcutaneously from the neck incision site to the generator in the chest pocket *after placement of the electrodes and anchor tether on the nerve, and placement of strain relief with the tie-downs.* (See "Place the Electrodes" and "Provide Strain Relief", respectively.)
2. After the bullet tip has passed from one incision site to the other, unscrew the bullet and withdraw the shaft from the sleeve, leaving the sleeve extended through both incisions (see Figure 18).

Figure 18. Position of Sleeve and Lead Connector(s)

Insert the lead into the sleeve at the neck incision until secure.



A Single-Pin Lead

B Tunneler Sleeve

C Dual-Pin Lead

3. With the sleeve in place between the two incisions, carefully insert the lead connector(s) inside the end of the sleeve at the neck incision. For a dual-pin lead, the second connector will form a slight compression fit between the first lead connector tubing and the inside of the sleeve (see Figure 18).
4. Carefully pull the sleeve, along with the lead connector(s), from the chest incision end until the lead connector(s) completely exit(s) the chest incision.
5. Remove the lead connector(s) from the sleeve, leaving the electrode array at the neck incision site.
6. Discard the tunneler after use.

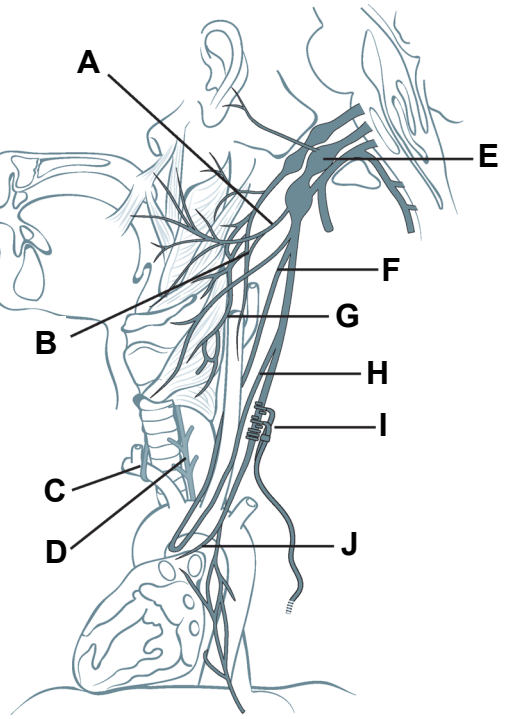
4.6.3 Place the Electrodes

4.6.3.1 Anatomy

It is very important that the surgeon implanting the VNS Therapy System be familiar with vagus nerve anatomy, particularly the cardiac branches. The lead electrodes must not be placed on either the superior or the inferior cervical cardiac branches. **Place the lead below where the superior and inferior cardiac branches separate from the vagus nerve.** Stimulation of either of these two branches during the System Diagnostics (Lead Test) may cause **bradycardia and/or asystole.** Careful dissection laterally on the vagus nerve should aid the physician in determining proper electrode placement. In most but not all patients, the main vagus nerve is the largest of the three nerves. Figure 19 shows the correct anatomical placement of the helices.

⚠ **Caution:** Attachment of lead electrodes must not involve the superior cervical cardiac branch or the inferior cervical cardiac branch of the vagus nerve. Place the electrodes *below* where these two branches separate from the vagus nerve.

Figure 19. Vagus Nerve Anatomy and Placement of the Lead



A Pharyngeal Branch of Vagus Nerve

B Communicating Branch of Vagus Nerve to Carotid Sinus Branch of Glossopharyngeal Nerve

C Right Recurrent Laryngeal Nerve

D Left Recurrent Laryngeal Nerve

E Left Vagus Nerve

F Superior Cervical Cardiac Branch of Vagus Nerve

G Superior Laryngeal Nerve

H Inferior Cervical Cardiac Branch of Vagus Nerve

I Lead Electrode Location

J Thoracic Cardiac Branch of Vagus Nerve

⚠ **Caution**: Excessive manipulation of the vagus nerve during placement of the lead can result in noticeable post-operative hoarseness. Under most circumstances, this condition will resolve without additional medical intervention within three to four weeks, depending on the degree of stress applied to the nerve during surgery. LivaNova does not recommend that stimulation treatment be initiated until this condition has resolved, since it could aggravate the condition.

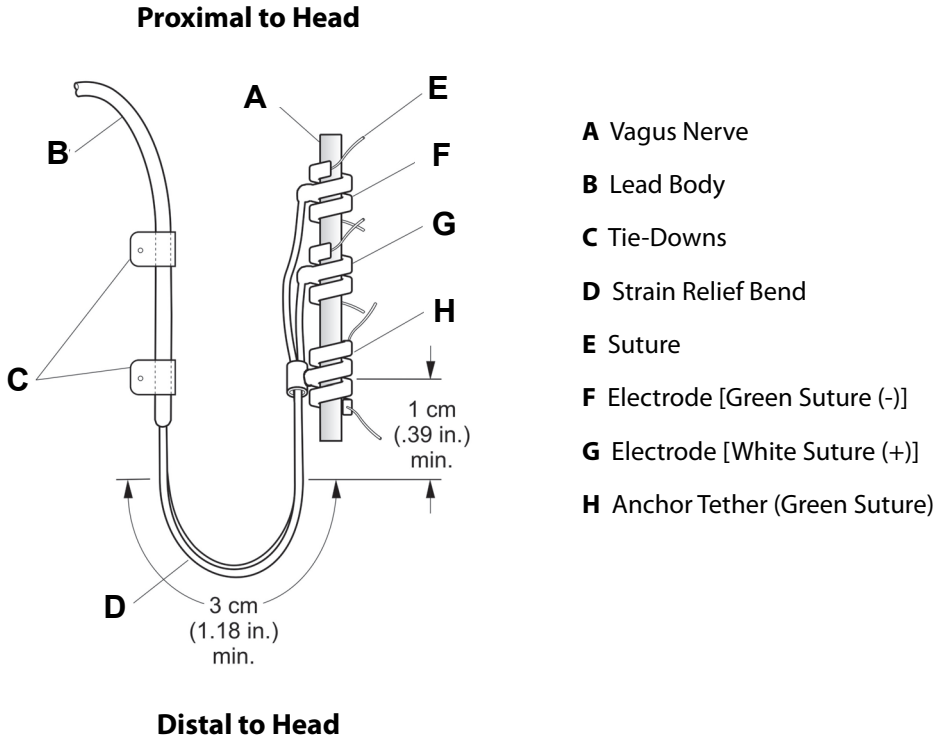
4.6.3.2 Electrode Polarity

The helical electrodes and anchor tether are coiled around the nerve, beginning with the electrode that is farthest from the lead bifurcation (with a green suture embedded in the helical material). This electrode should be nearest (proximal to) the patient's head.

⚠ **Caution: The lead and helical electrodes are very delicate**; be careful not to stretch, pinch, or crush them when using forceps, and not to over-straighten or stretch the helices when coiling them around the nerve, because doing so may damage the electrode or tether. Use soft rubber vessel loops to raise, or lift, the nerve, if necessary.

Depending on the surgeon's preference, the helices can alternately be placed by putting the anchor tether on first (distal to head), next placing the electrode closest to the lead bifurcation (with white suture), and then placing the electrode farthest from the lead bifurcation (with green suture). The polarity of stimulation does not change (see Figure 20).

Figure 20. Electrode Polarity



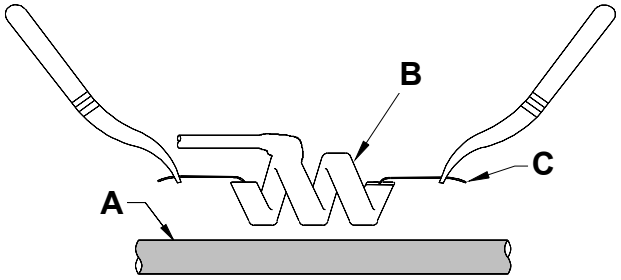
4.6.3.3 Place the helicals around the nerve

The helicals can be placed on the nerve as described below. As an alternative, each helical can be placed underneath the nerve before it is spread. A silicone sheet may be useful to separate the nerve from tissue during the procedure.

1. Locate the first helical (with green suture).
2. With forceps, gently pull each end of the helical, using the attached sutures to spread the helical (see Figure 21).

⚠ **Caution:** The suture may become dislodged from the helical if product labeling is not followed (i.e., grasping the elastomer and suture to manipulate the helical onto the nerve).

Figure 21. Spread the Helical



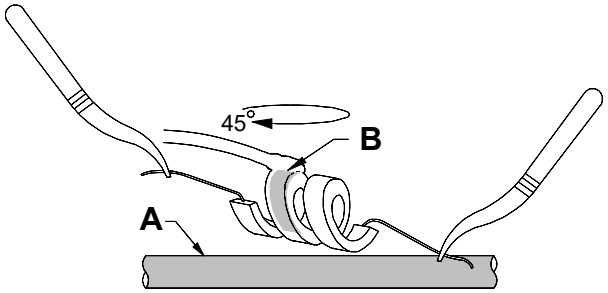
A Nerve

B Helical

C Suture

3. Spread the opened helical directly above and parallel to the exposed nerve and turn the helical clockwise at a 45 degree angle to the nerve (see Figure 22).

Figure 22. Turn the Helical

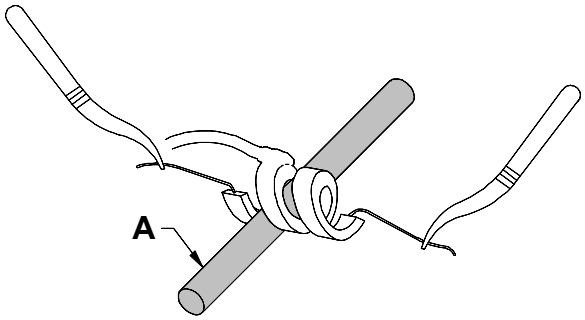


A Nerve

B Metal Ribbon

4. Place the turn of the helical where the lead wire connects to the helical (the section with the metal ribbon) onto the nerve (see Figure 23).

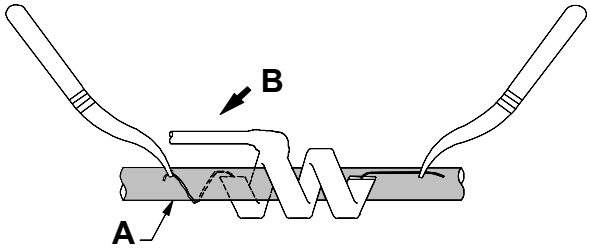
Figure 23. Placement of the Turn



A Nerve

5. Pass the *distal* suture portion of the helical under the nerve and back around so that it encircles the nerve (see Figure 24 and Figure 25).

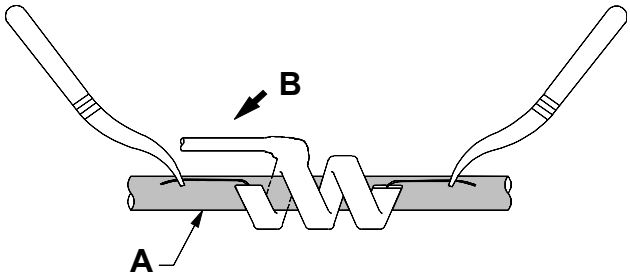
Figure 24. Initial Placement of the Distal Portion of the Helical



A Nerve

B Distal to Head

Figure 25. Helical Placement After Distal Portion Encircles the Nerve

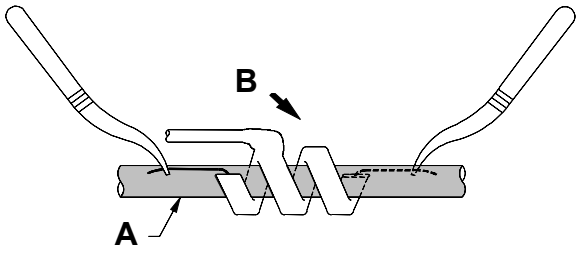


A Nerve

B Distal to Head

6. Pass the *proximal* suture portion of the helical under the nerve and back around so that it encircles the nerve (see Figure 26).

Figure 26. Placement of the Proximal Portion of the Helical



A Nerve

B Proximal to Head

7. Locate the middle helical (with white suture) and repeat steps 2 - 6.
8. Locate the third helical (with green suture) and repeat steps 2 - 6.
9. Verify all three helices have been coiled around the nerve, the lead body exits each helical in the same direction, and the two lead bodies are aligned parallel to each other and the nerve. The correct placement of the two helical electrodes and anchor tether is shown in Figure 27.

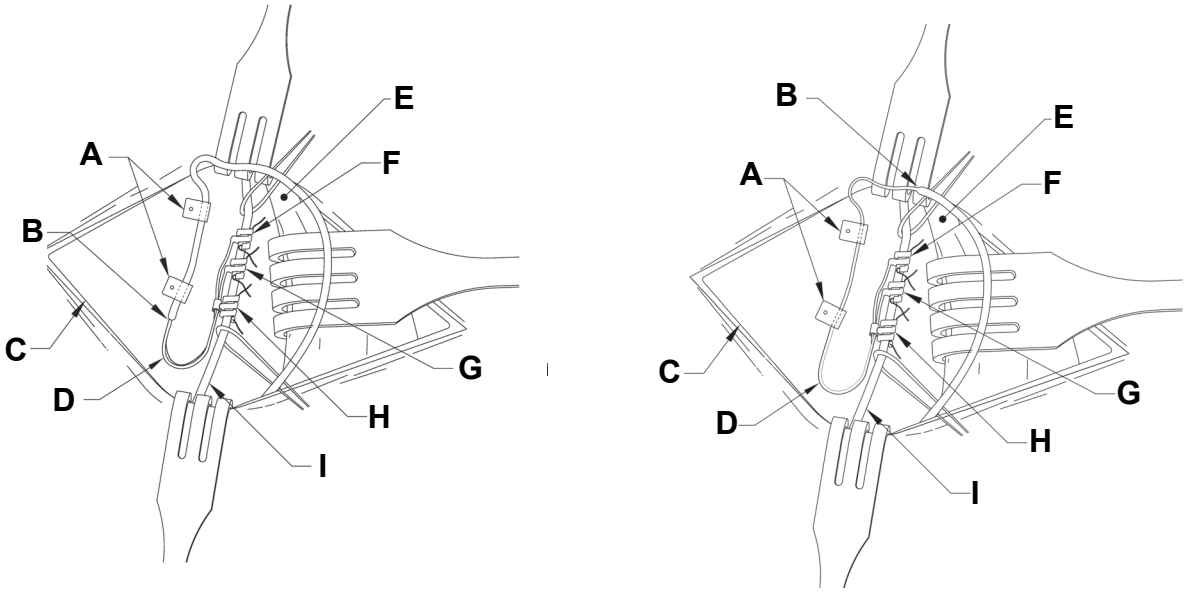
⚠ **Caution:** Sutures that are part of the lead (embedded in the helices of the electrodes and anchor tether) are meant to assist in helical placement around the vagus nerve. These sutures should not be tied to each other or around the nerve, since this may cause nerve damage.

⚠ **Caution: Proper techniques** for attaching the electrodes and the anchor tether to the left vagus nerve are critical to the long-term success of the implant.

Figure 27. Placement of Electrodes and Anchor Tether

302 and 304 Lead **303 Lead**

Proximal to Head



Distal to Head

A Sutured Tie-Downs

B Lead Transition

C Neck Incision

D Strain Relief Bend

E Sternocleidomastoid Muscle

F Electrode Farthest From Lead Transition [Green Suture (-)]

G Electrode [White Suture (+)]

H Anchor Tether (Green Suture)

I Vagus Nerve

4.6.4 Provide Strain Relief

⚠ **Caution: Proper techniques** for providing adequate strain relief below and above the sternocleidomastoid muscle are critical to the long-term success of the implant.

⚠ **Caution: The lead wire has a potential for fracture** if the recommended strain relief is not provided as described.

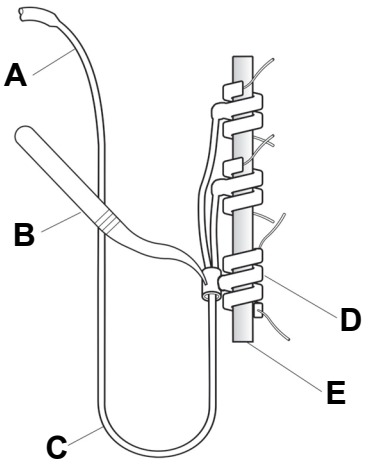
After attaching the two electrodes and the anchor tether, form a strain relief bend and a strain relief loop in the lead to provide adequate slack and allow for neck movement.

4.6.4.1 Form the strain relief bend

To form the *strain relief bend* (see Figure 17, Figure 28 [303 only], and Figure 29), do the following:

1. Form the lead body into a 3-cm (1.18 in) strain relief bend with at least 1 cm (0.39 in) of lead routed parallel to the nerve. (303 lead only—Pay careful attention to the previously placed anchor tether and electrodes so they do not come unattached. Slight pressure may be placed against the anchor tether with a surgical instrument to ensure support to the anchor tether while the strain relief bend is being formed [see Figure 28]). The parallel portion can be placed in a pocket formed adjacent to the anchor tether.

Figure 28. (*303 Lead only*) Use of Surgical Tool (e.g., forceps) to Support Anchor Tether During Strain Relief Formation



A Lead

B Surgical Tool

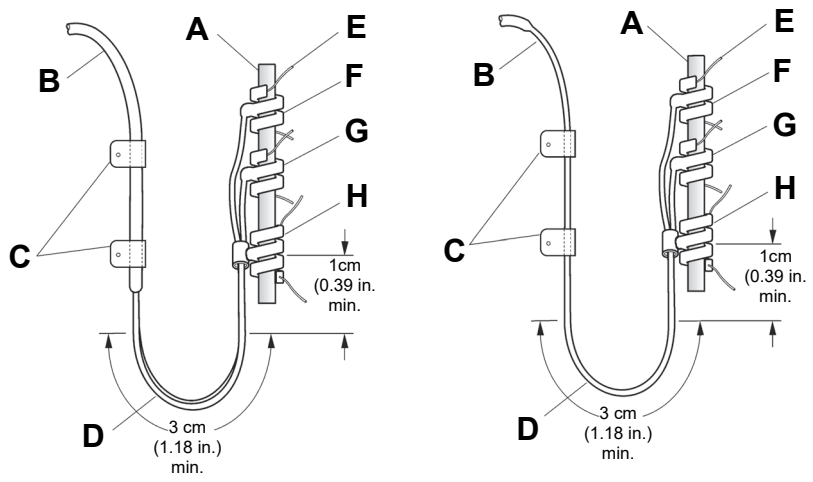
C Strain Relief Bend

D Anchor Tether (Green Suture)

E Vagus Nerve

2. Loosely attach the 3-cm strain relief bend to the adjacent fascia with tie-downs before routing the lead over the muscle. The first tie-down should be positioned laterally to the anchor tether (see Figure 29). Four (or more) tie-downs are provided in the lead sales pack.

Figure 29. Use of Tie-downs in Electrode Placement



A Vagus Nerve

B Lead Body

C Tie Downs

D Strain Relief Bend

E Suture

F Electrode [Green Suture (-)]

G Electrode [White Suture (+)]

H Anchor Tether (Green Suture)

⚠ **Caution:** Sutures that are part of the lead coil are meant to assist in electrode placement around the left vagus nerve. These sutures should *not* be tied to each other since this may cause nerve damage (see Figure 29).

⚠ **Caution: The lead and its electrodes are very delicate,** and care should be taken not to over stretch or crush the helices.

4.6.4.2 Form the strain relief loop

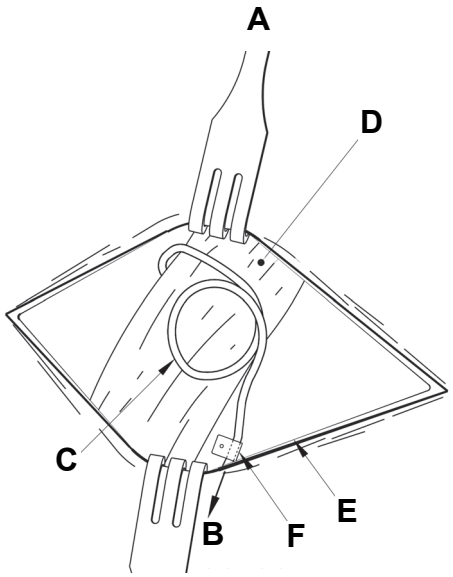
To form the *strain relief loop* (see Figure 30), do the following above the sternocleidomastoid muscle:

1. In the neck, form the lead into a large subcutaneous loop.
2. Loosely attach it to fascia with a tie-down before routing the lead over the clavicle. This strain relief loop should be large enough to provide several inches/centimeters of lead extension when the neck is turned to its maximum stretched positions.

⚠ **Caution: Leave enough extra lead** on both sides of the clavicle to prevent the tension over the clavicle from damaging the lead.

⚠ **Caution:** Placing the sutures directly on the lead body may result in insulation damage or wire failure, causing premature failure of the lead. Use only supplied tie-downs to secure the lead.

Figure 30. Strain Relief Loop



A Proximal To Head

B To Clavicle

C Strain Relief Loop

D Sternocleidomastoid Muscle

E Neck Incision

F Tie-Down

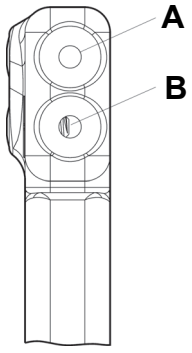
4.7 Connect the Lead to the Generator

⚠ **Caution**: Do not use electrosurgical equipment after the generator has been introduced to the sterile field. Exposure to this equipment may damage the generator.

To connect the lead directly to the generator:

1. Look inside the generator lead receptacle(s) to verify that no obstruction exists and that the setscrew(s) has been backed out adequately to allow full insertion of the connector pin(s). Avoid backing the setscrew(s) out further than needed for lead insertion (see Figure 31). The figure is intended to show the contrast between a blocked and a clear receptacle, and applies to single or dual pin headers.

Figure 31. Generator Receptacle and Setscrew



A Receptacle Hole Clear

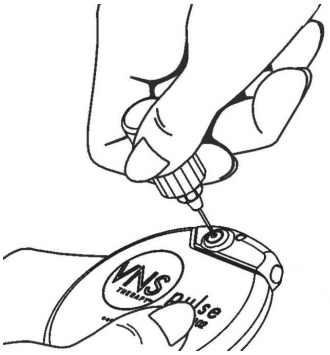
B Setscrew Visible (Manually back out)

2. Keep the hex screwdriver perpendicular to the generator. Insert the hex screwdriver through the center of the setscrew plug(s) to vent back pressure accumulated during lead insertion.

⚠ **Caution:** In the steps below, **always push down on the hex screwdriver while turning it clockwise until it clicks** (begins ratcheting) while ensuring that it is fully inserted in the setscrew. Also, the hex screwdriver must be inserted into the center of the silicone rubber setscrew plug and kept perpendicular to the generator to avoid stripping the setscrew and/or dislodging the setscrew plug.

⚠ **Caution:** When using the hex screwdriver, grasp it by the handle only, as shown in Figure 32. Do not grasp any other portion of the hex screwdriver during use, as this may affect its proper function. Touching the metal shaft while the hex screwdriver is engaged with the setscrew can conduct an electrostatic discharge into the device circuitry and may damage the generator.

Figure 32. Hex Screwdriver Position



3. When using a **single-receptacle** generator and VNS Therapy single-pin lead, insert the lead connector pin fully into the generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug.

When using a **dual-receptacle** generator and VNS Therapy dual-pin lead, insert the lead connector pins fully into the appropriate lead receptacles in the generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug of the connector being inserted. Insert the lead connector with the white marker band and with the embedded model number and serial number tag into the lead receptacle labeled "+" (see the Dual-Receptacle generator portion of Figure 33). The remaining lead connector is inserted into the remaining lead receptacle.

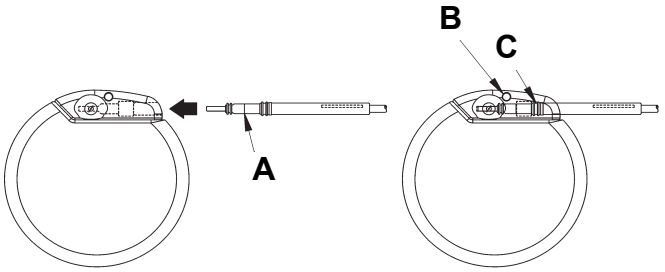
⚠ **Caution:** To avoid backing the setscrew out completely when loosening, during surgery, use no more than two counterclockwise turns.

⚠ **Caution: Reversal of lead polarity has been associated with an increased chance of bradycardia** in animal studies. It is important to make sure that the lead connector pins in the VNS Therapy dual-pin lead are correctly inserted (white marker band to + connection) into the generator dual receptacles.

Figure 33. Lead Connector(s) Prior to Insertion and Fully Inserted

Single-Receptacle Generator

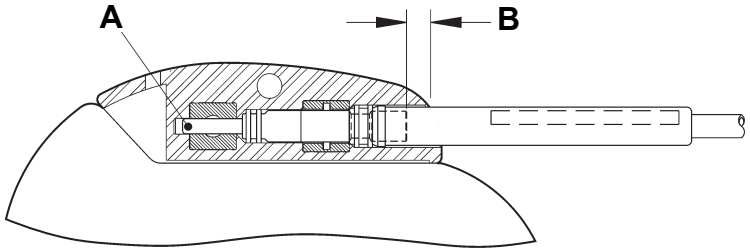
Prior to Insertion **Fully Inserted**



A Lead

B Suture Hole - Always suture to fascia

C Insert fully

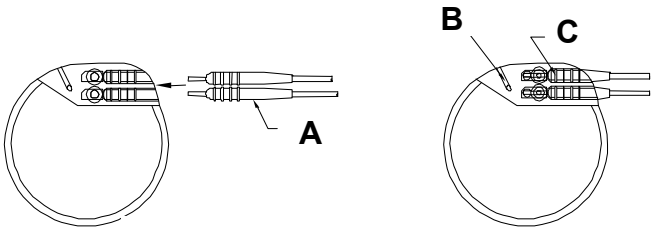


A End of connector pin should be visible in cavity

B Be sure end of connector ring is inside of lead receptacle

Dual-Receptacle Generator

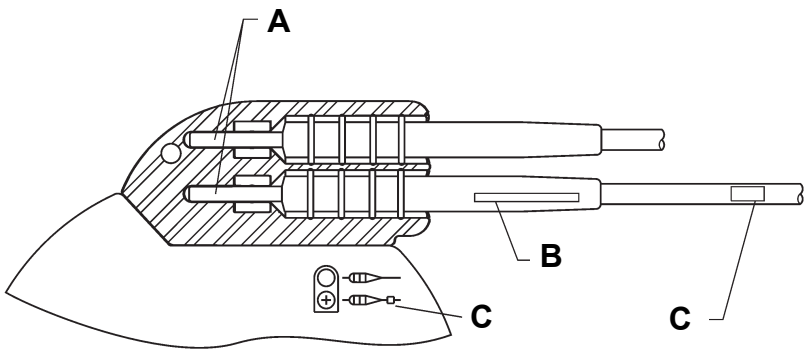
Prior to Insertion **Fully Inserted**



A Lead

B Suture Hole - Always suture to fascia

C Insert fully



A Make sure connector pins are fully inserted

B Serial Number Tag

C White Marker Band

4. With the hex screwdriver still inserted through the setscrew plug, verify that the connector pin is fully inserted. The pin should be visible in the area at the back end of the setscrew connector block. If it is not, remove the pin. To loosen the setscrew, engage the hex screwdriver into the setscrew, and turn it counterclockwise until the

connector pin can be fully inserted. Avoid backing the setscrew out further than needed for lead insertion. If using the dual-receptacle generator, repeat this procedure for each setscrew.

5. After verifying that the connector pin(s) has been fully inserted, tighten each setscrew by engaging the setscrew with the hex screwdriver and turning the hex screwdriver clockwise until it begins to click. Always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

⚠ **Caution:** It is important to do the following:

- Ensure that the lead receptacle(s) is clean and free of obstruction.
- Carefully insert the lead connector pin(s) into the lead receptacle(s) without bending the lead connector(s).
- Visually inspect that the connector pin(s) is clean and completely inserted.
- **Electrical connection to the generator is not established until the setscrew(s) is completely tightened with the hex screwdriver.** Failure to make a good connection can result in HIGH impedance during a System Diagnostics (Lead Test) or erratic stimulation at varying intensity due to rapid, unpredictable changes in lead impedance, which is expected to adversely affect device effectiveness and may have serious safety consequences. Additionally, for generators capable of tachycardia detection, heartbeat sensing may be compromised.
- Gently grasp and pull on lead connector boot(s) (the thick section of the lead) to verify the lead is properly secured inside the lead receptacle(s). Do not pull on lead body (thin section) or use excessive pull force, because doing so may cause lead damage.

4.8 Test the VNS Therapy System

The System Diagnostics (Lead Test), which should be conducted first, is performed with the lead and the generator connected. Thus, if the System Diagnostics (Lead Test) is successful, both components are working properly. However, if the System Diagnostics (Lead Test) fails, either of the two components could be defective, or there may not be a good electrical connection between the generator and the lead connector pin(s). If a defective component is suspected, disconnect the lead and perform the optional Generator Diagnostics (Pre-Implant Test), using the resistor assembly supplied with the accessory pack.

ⓘ **Note:** The programming wand should be placed into a sterile laser arm bag or equivalent (not provided by LivaNova) in order to introduce the programming wand into the sterile field. See the programming system physician's manuals for more information.

⚠ **Caution:** During the intraoperative System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. If a patient has experienced asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate during a System Diagnostics (Lead Test) at the time of initial device implantation, the patient should be placed on a cardiac monitor during initiation of stimulation.

The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.

4.8.1 System Diagnostics (Lead Test)

The System Diagnostics is performed intraoperatively when the lead and the generator are connected. The test checks the connection between the lead, generator, and the nerve. Depending on the generator model and programmed Normal Mode output current, different test pulses may be conducted during the test (see Table 24).

Table 24. System Diagnostics (Lead Test)

<table>
<tr><th rowspan="2">Normal Mode Output Current</th><th colspan="3">System Diagnostics Behavior</th></tr>
<tr><th>M102/102R</th><th>M103-106</th><th>M1000/1000-D</th></tr>
<tr><td>0 mA</td><td rowspan="2">1 mA, 500 µsec for approximately 14 seconds</td><td>1 mA, 500 µsec for approximately 14 seconds</td><td rowspan="2">Delivery of programmed output for approximately 4 seconds, followed by one brief pulse at 0.25 mA for less than 130 µsec,*</td></tr>
<tr><td>>0 mA</td><td>One brief pulse at 0.25 mA, 130 µsec, followed by delivery of programmed output for the duration of the programmed ON time.</td></tr>
</table>

* Minor differences in the system diagnostics test exist for M1000 with serial numbers <100,000. Refer to the *Introduction to the VNS Therapy System* chapter for more information.

Note: Once programmed ON, lead impedance measurement readings are automatically performed once every 24 hours for Model 103 and higher generators.

To ensure proper system connection and functionality, perform the test and assess the following:

- Model 102/102R: Verify that the lead impedance status is "OK".

  Note: See the programming system physician's manuals for lead impedance details.

- Model 103-1000/1000-D: Verify that System Diagnostics is successful (output current and lead impedance are "OK").

If lead impedance status is not "OK" for Model 102/102R, or if the System Diagnostics fails for Model 103-1000/1000-D (output current "LOW" or lead impedance "HIGH" or "LOW") see "Troubleshooting" in the programming system physician's manuals.

Caution: Electrical connection between the generator and the lead connector pin(s) may be at fault.

4.8.2 Generator Diagnostics (Pre-Implant Test)

The optional Generator Diagnostics is performed when the test resistor is attached to the generator in cases of troubleshooting. When the System Diagnostics fails (lead impedance "HIGH" or "LOW"), the Generator Diagnostics can be used to determine whether the lead or the generator is causing the problem. The Generator Diagnostics is performed with the test resistor that is included in the accessory pack. This test will verify that the generator is functioning properly, independent of the lead.

To connect the test resistor to the generator, perform these steps:

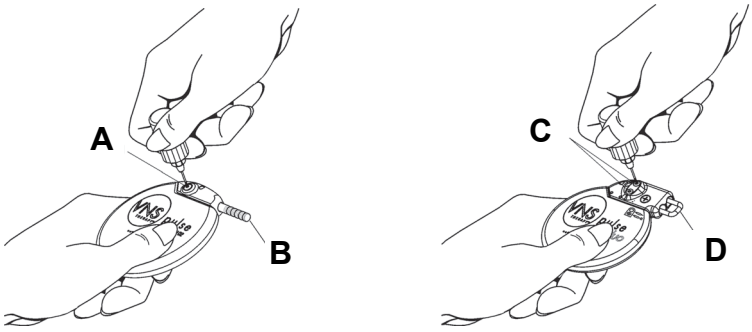
1. Remove the lead connector pin(s) from the lead receptacles by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than a half-turn should be required to remove the lead.
2. Insert the connector pin(s) of the resistor assembly into the lead receptacle(s). Be careful while inserting the test resistor pin(s) into the lead receptacle(s). If binding or significant resistance is felt, remove the test resistor, inspect it, and clean it if necessary. Without the use of excessive force, reinsert the test resistor.

Note: Fully insert the hex screwdriver into the setscrew and push in on the hex screwdriver whenever the setscrew(s) is being tightened or loosened.

3. When the resistor assembly is in place, tighten the setscrew(s) until the hex screwdriver begins to click (see Figure 34). Again, always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

Figure 34. Connect the Resistor Assembly

Single-Receptacle Generator **Dual-Receptacle Generator**



A Setscrew Plug

B Resistor Assembly

C Setscrew Plugs (2)

D Resistor Assembly

4. Perform the Generator Diagnostics (Pre-Implant Test).

- If the Generator Diagnostics (Pre-Implant Test) is successful (lead impedance "OK"), the generator is working properly.
- If the Generator Diagnostics fails (lead impedance "HIGH" or "LOW"), see "Troubleshooting" in the programming system physician's manuals.
- If the component is damaged, contact LivaNova and return the item (following the disinfection procedure described in the "Precautions" section of the *Introduction to the VNS Therapy System* chapter), along with a completed Returned Product Form.

Note: See the programming system physician's manuals for details.

4.8.3 Optional Monitoring

Optional physiologic monitoring of VNS Therapy System operation may be done if surgery is performed under local anesthesia. Monitor the patient's voice for signs of hoarseness while gradually increasing the generator output current. After performing the System Diagnostics and obtaining successful results, reset the current to 0 mA.

4.8.4 Heartbeat Detection and Tachycardia Detection Configuration

For generators capable of tachycardia detection, configure the heartbeat detection and tachycardia detection functions after the diagnostic testing is complete:

1. Place the generator in the chest pocket, coiling the remaining slack of the lead and placing it to the side of the generator. The generator can be placed with either side facing outward.
2. Use the programming software to turn on tachycardia detection and verify heartbeat detection.

   Note: Steps for configuring tachycardia and heartbeat detection are software specific. See the programming system physician's manuals for details.

3. Use the following method to select a patient-specific **Heartbeat Detection** (sensitivity) value:

   - Average the two R-wave amplitude measurements obtained from the positional assessment. If this information is not available, go to step 6.
   - Map the average R-wave amplitude value to the appropriate Heartbeat Detection setting in Table 25 and select this value in the programming software.

   Note: To determine R-wave amplitude, see Step 6 in the "Determine acceptable device implant locations (tachycardia detection only)" section.

Table 25. Heartbeat Detection Mapping

Heartbeat Detection	Average Amplitude (mV) (across different postures)	
	Minimum	Maximum
5	0.40	0.50
4	0.51	0.70
3	0.71	0.85
2	0.86	1.25
1	1.26	--

4. During the heartbeat detection verification process, the programming software will display the heart rate detected by the generator for 2 minutes. The process will automatically stop after 2 minutes, or you may manually stop the process by pressing "Stop". The wand must stay over the generator during the entire process.
5. During the heartbeat detection verification process, use the ECG monitor to compare the heartbeat reported on the programming computer with that reported by the ECG monitor. If heartbeat detection is accurate, go to Step 8, Otherwise, go to Step 6.

6. If heartbeat detection is inaccurate in Step 5, or if the R-wave amplitude information from the "Determine acceptable device implant locations (tachycardia detection only)" section is not available, select a value of "1" from the Heartbeat Detection parameter list (1-5) and repeat steps 4 - 5.
7. Monitor and compare the heartbeat reported on the programming computer with that reported by the ECG monitor, and repeat Steps 4 - 5, as necessary, to test or configure other Heartbeat Detection settings (settings 2, 3, 4, 5) until the device accurately detects heartbeats. If more than one heartbeat detection setting results in accurate detection of heartbeats, select the lesser of these detection settings.
8. Select the **AutoStim Threshold** as appropriate (70%-least sensitive, 20%-most sensitive) and apply changes (i.e., program).
9. After configuration, proceed to "Complete the Implantation Procedure", step 2.

4.9 Complete the Implantation Procedure

⚠ **Caution:** Do not place the lead slack under the generator, because doing so could result in insulation failure and system malfunction.

⚠ **Caution:** This suturing is important to stabilize the generator and to prevent manipulation by the patient, which could damage the lead wires.

⚠ **Caution:** Do not place the sutures directly around the body of the lead; this could result in insulation failure and system malfunction, and possible lead breakage.

After the testing has been completed, finish the implantation procedure:

1. Place the generator in the chest pocket, coiling the remaining slack of the lead and placing it to the side of the generator. The generator can be placed with either side facing outward.
2. Secure the generator by placing a suture through the suture hole and attaching it to fascia (not to muscle).
3. Perform the second System Diagnostics and verify lead impedance status remains "OK."
4. Interrogate the generator to verify that Normal Mode, Magnet Mode, and AutoStim Mode (*106 and 1000/1000-D generators only*) output is 0 mA.
   - Output current: 0 mA
   - Magnet current: 0 mA
   - AutoStim current: 0 mA

   ⚠ **Caution: Do not program the generator to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.** Failure to observe this precaution may result in patient discomfort or adverse events.

5. LivaNova recommends irrigation of both incision sites with generous amounts of bacitracin or equivalent solution before closure.
6. Close the surgical incisions. Use cosmetic closure techniques to minimize scarring.
7. Administer antibiotics postoperatively (at the discretion of the physician).

A neck brace can be used by the patient for the first week to help ensure proper lead stabilization.

4.10 Post Implant Patient Identification and Materials

4.10.1 Implant Warranty and Registration Form

Included with the generator is an Implant Warranty and Registration Form that *must* be completed and the top, white copy returned to LivaNova. Give a copy of this form to the patient or caregiver.

This information, as required by government agencies, becomes part of the LivaNova registry of implantees and is used as a permanent record of implant recipient information.

4.10.2 Patient Magnet Kit

Give the patient a Patient Magnet kit, which contains magnets, accessories, and other patient materials.

4.10.3 Patient Implant Card

The implant card contains information about the patient's VNS Therapy System. Give the card(s) to the patient and/or caregiver after the implant and tell them to complete it with their device information (if not already included), the patient's name, or other identifying information (e.g. patient number) and their treating physician's name and phone number. Tell them to carry it with them at all times.

5 Epilepsy Information—Patient Follow Up

5.1 Guidelines for Patient Follow Up

5.1.1 After Implantation

During the first few weeks after implantation of new or replacement devices, the patient should be seen to confirm wound healing and proper generator operation. The generator's output current for the programmed stimulation in all modes must be 0 mA for the first 14 days after implantation.

The VNS Therapy System is an adjunctive therapy to existing (prior to device implantation) antiepileptic medications. Physicians are encouraged **to keep all antiepileptic medications stable for the first three months** of stimulation before attempting to reduce or change a patient's medication.

5.1.2 Follow-up Visits

5.1.2.1 Initial titration visits (ramping up VNS Therapy)

During initial programming, the patient may be seen more frequently to make adjustments in therapy until a target level (i.e., adequate seizure control with minimal side effects) is reached. Once stimulation is ready to be programmed ON, the output current should be slowly increased in 0.25 mA increments until the patient feels the stimulation at a comfortable level. Patients who are receiving replacement generators should also be titrated in the same manner to allow re-accommodation. See "Dosing Strategies" for more information.

Note: (*Generators with AutoStim only*) A smaller output current step size of 0.125 mA is available (up to 2 mA) to allow for patient tolerability to device stimulation.

5.1.2.2 Long-term follow up

The subsequent follow-up schedule and the nature of each examination should be determined by the physician on the basis of patient response to and tolerance of the implant. In all other respects, follow up should be performed in accordance with the standard medical practice for patients with epilepsy.

In the event intolerable adverse events are reported, physicians should always try reducing stimulation parameters as a means of eliminating or reducing the severity of an event. See "Tolerability Strategies" for parameter adjustment recommendations. Additionally, physicians should instruct patients or caregivers on the application of the magnet to turn the generator off (output current 0 mA) if an adverse event becomes intolerable.

5.1.2.3 Typical follow-up visit activities

At each patient visit, the generator should be interrogated, using the appropriate version of the VNS Therapy programming software. Stimulation adjustments may also be performed depending on patient response and/or tolerability.

VNS Therapy System treatment should not be uncomfortable, nor should it cause bothersome side effects. Patients may be observed after the last stimulation adjustment to make certain that they are comfortable with all available programmed stimulation modes. Since each

patient may respond differently to the stimulation, the observation period may be at least 30 minutes, or as long as necessary as determined by the physician.

Diagnostic testing should also be performed at each visit to confirm proper functioning of the VNS Therapy System. Additionally, it is recommended that testing of the magnet output be performed while the patient is still in the physician's office to ensure tolerability of the Magnet Mode output.

For generators with AutoStim Mode, heartbeat detection performance should be evaluated at each visit.

After reprogramming and/or diagnostics testing, data should be printed out and filed. These data can be used for comparison with a patient's diary or own records to evaluate the VNS Therapy System, to confirm proper VNS Therapy System functioning, and to assess the need for reprogramming. At the end of the session, a final interrogation should be performed to confirm parameters are set to the intended dose before the patient leaves the office.

Note: For instructions on printing out data, see the programming system physician's manuals.

5.2 Individualization of Treatment

5.2.1 Therapy Parameters Used in Clinical Trials

The average output current used during the clinical studies after 3 months of stimulation was about 1 mA.[1] Other standard Normal Mode treatment settings were 30 Hz, 500 µsec pulse width, 30 seconds ON time, and 5 minutes OFF time. There are no data to verify that these are optimal parameters.

Caution: (*Generators with AutoStim only*) It is recommended that the output current for the AutoStim Mode not exceed the greater of output current for the Normal Mode or Magnet Mode, especially for patients who experience discomfort or adverse stimulation effects (e.g., during sleep).

Caution: (Model 106 Serial Numbers < 80000 only) Magnet Mode output current should be set at least 0.125 mA higher than AutoStim output current, to prevent rare instances where a device safety feature disables stimulation due to repeated magnet applications.

Table 26 lists the range of stimulation parameters after 3 months of active treatment used in the randomized, blinded, active control trials.

[1] Heck C., Helmers SL, DeGiorgio CM. "Vagus nerve stimulation therapy, epilepsy, and device parameters: scientific basis and recommendations for use". *Neurology* 2002; 59 (6, Suppl 4): S31-7.

Table 26. High Stimulation Group Parameters

Stimulation Parameters	Normal Mode	Magnet Mode
Output current	0–3.5 mA	0–3.5 mA
Frequency	30 Hz	30 Hz
Pulse width	500 µsec	500 µsec
ON time	30 sec	30 sec
OFF time	5 min	N/A

There is no proven correlation at present between high output current (mAmps) and device effectiveness, nor is there a standard treatment level that needs to be achieved during treatment ramping. However, computational modeling of vagus nerve stimulation suggests an approximate target for nerve activation.[1]

5.2.2 Dosing Strategies

In general, VNS Therapy should be set to a comfortable level for the patient and increased as tolerated to help achieve efficacy. Although LivaNova recommends adjusting output current as necessary, there are no controlled data at this time to indicate that higher current levels are associated with better efficacy. Patients whose seizures are well controlled at follow up should not have their settings changed unless they experience uncomfortable side effects.

Patients should be started on stimulation at a low current setting (0.25 mA), and the current should be increased gradually to allow accommodation to the stimulation. For patient comfort, the output current should be increased in 0.25 mA increments until a comfortable tolerance level is reached. Physicians should appreciate that some patients will accommodate to stimulation levels over time and should therefore allow further increases (in 0.25 mA steps) in output current, if needed.

Note: The Guided Programming feature in select versions of the VNS programming software can help guide you through the initial titration process. See the programming system physician's manuals for details.

The magnet output should be programmed at each visit, if necessary, to a level that is perceptible to the patient. This is typically set 0.25 mA higher than the Normal Mode output current. Some patients have reported that it is easier to verify daily that stimulation is being delivered if the magnet output current is set to one step above normal stimulation settings. This slightly higher output current is intended to allow patients who have accommodated to normal stimulation to recognize or perceive the magnet stimulation, thereby confirming device function.

For generator models with AutoStim, the AutoStim output current should be set no greater than the Magnet Mode output current. You may choose to set AutoStim output current between the Normal and Magnet Mode output currents, or equal to Normal Mode for comfort or tolerability.

Caution: (Model 106 Serial Numbers < 80000 only) Magnet Mode output current should be set at least 0.125 mA higher than AutoStim output current, to prevent rare instances where a device safety feature disables stimulation due to repeated magnet applications.

[1] Helmers SL, Begnaud J, Cowley A, et al. "Application of a computational model of vagus nerve stimulation". *Acta Neurol Scand.* 2012; 126 (5): 336-43.

Table 27 lists the suggested initial stimulation parameters to begin titration of VNS Therapy.

Table 27. Suggested Initial Stimulation Parameters (≥ 2 Weeks After Implant)

NORMAL	Output Current	0.25 mA
	Signal Frequency†	20 - 30 Hz
	Pulse Width†	250 - 500 µsec
	Duty Cycle: 10%	
	Signal ON Time	30 sec
	Signal OFF Time	5 min
AUTOSTIM*	Output Current	0.25 - 0.375 mA
	ON Time	60 sec
	Pulse Width	250 - 500 µsec
MAGNET	Current	0.5 mA
	ON Time	60 sec
	Pulse Width	250 - 500 µsec

* Not available in all generator models.

† Some patients may find 20 Hz/250 µsec more tolerable. For this reason, some physicians prefer to start at the lower settings, and increase as tolerable. Other physicians may prefer to start at the higher settings, and adjust downward if needed for tolerability (Heck, Helmers, and DeGiorgio. 2002).

5.2.3 Tolerability Strategies

After each output current increase, evaluate the patient for tolerability. If an increase in output current is not tolerable, other stimulation parameters may be adjusted as shown in Table 28 to help with patient tolerability.

Prior to each parameter adjustment, it is recommended to revert the output current to the last level that was tolerated by the patient.

Make the parameter adjustment and try the increase in output current again.

If the patient was already started at the lower recommended settings for pulse width and frequency, reductions in output current and further reductions in pulse width may be the only course of action. However, if the pulse width is reduced to 130 µsec, the output current should be increased to minimize the impact to the overall amount of therapy delivered. Literature has

shown that a higher output current is needed to activate the vagus nerve when pulse widths below 250 µsec are used.[1] & [2]

Table 28. Parameter Adjustments for Tolerability[3]

Parameter	Adjustment
Pulse Width	500 → 250 µsec
Signal Frequency	30 → 20 Hz*
Output Current	↓ 0.125 mA† or ↓ 0.25 mA

* 25 Hz is also available

† Only available in certain generator models

Table 29 provides an example of how to titrate when adjusting for patient comfort. Each example includes what the starting signal frequency and/or pulse width might be.

Table 29. Example — Tolerability Adjustments During Titration

Programming Steps	Parameter	Adjustment	Purpose
1	Output Current	+0.25 mA	Titration attempt
If patient experiences discomfort:			
2	Output Current	-0.25 mA	Comfort adjustment
3	Pulse Width or Signal Frequency	500 → 250 µsec or 30 → 20 Hz	
If parameter reduction is tolerable, continue titration.			
4	Output Current	+0.25 mA	Titration attempt

If the output currents are reduced to address side effects, but the target level (i.e., adequate seizure control with minimal side effects) has not been reached, future attempts at increasing output current are recommended.

5.2.4 Example Dosing Approach

This section describes a 2-phase dosing approach.[4] The goal of Phase 1 (0.5-3 months after implant) is to increase the output current to a target range. The goal of Phase 2 (3-18 months

[1] Koo B, Ham SD, Sood S, Tarver B. "Human vagus nerve electrophysiology: A guide to vagus nerve stimulation parameters". *J Clin Neurophysiol* 2001;18 (5): 429-33.

[2] Helmers SL, Begnaud J, Cowley A, et al. "Application of a computational model of vagus nerve stimulation". *Acta Neurol Scand.*2012; 126 (5):336-43.

[3] Heck C, Helmers SL, DeGiorgio CM. "Vagus nerve stimulation therapy, epilepsy, and device parameters: Scientific basis and recommendations for use". *Neurology* 2002; 59 (6, Suppl 4):S31-7.

[4] Heck C, Helmers SL, DeGiorgio CM. "Vagus nerve stimulation therapy, epilepsy, and device parameters: Scientific basis and recommendations for use". *Neurology* 2002; 59 (6, Suppl 4):S31-7.

after implant) is to increase the duty cycle. If the patient achieves desired outcomes at any point, further adjustments may be stopped.

5.2.4.1 Phase 1 (output current)

Note: The Guided Programming feature in select versions of VNS programming software can help guide you through Phase 1 of this dosing approach. See the programming system physician's manuals for details.

Two weeks following implantation surgery, apply the initial recommended settings as described in Table 27. You may choose to start the pulse width and frequency at 500 µsec and 30 Hz respectively, and adjust down as needed for tolerability. Or, you may start at the lower range of the recommended settings, 250 µsec and 20 Hz.

With a duty cycle of 10%, increase the output current upward in 0.25 mA steps over the next several weeks. The target for output current is 1.5-2.25 mA depending on pulse width selection:[1]

- 1.5 mA if PW 500 µsec
- 1.75 mA if PW 250 µsec
- 2.25 mA if PW 130 µsec

Multiple step (0.25 mA) increases can be made in output current during a single visit if tolerated by the patient. Frequent visits during this titration phase may allow for faster progress toward the target output current. Table 30 shows how all three stimulation modes can be adjusted:

Table 30. Output Current Adjustments

Mode	Step 1	Step 2	Steps 3, 4, 5 ...	Target*
Normal (mA)	0.25	0.50	+0.25	1.5- 2.25
AutoStim (mA)†	0.375	0.625	+0.25	1.625 - 2.25†
Magnet (mA)	0.50	0.75	+0.25	1.75 - 2.5

* Target output current depends on pulse width selection. See combinations above.

† AutoStim Mode is not available for all generator models. Output currents for AutoStim Mode may be set in between Normal and Magnet mode selections (as shown), or equal to the Normal Mode for comfort or tolerability.

5.2.4.2 Phase 2 (duty cycle)

Once the output current has reached the target, duty cycle may be adjusted upward to assess better patient response. Allow adequate time between duty cycle adjustments for patient evaluation. Adjustments to duty cycle should be less frequent (approximately 3-6 months). Table 31 shows the recommended duty cycle increases.

[1] Helmers SL, Begnaud J, Cowley A, et al. "Application of a computational model of vagus nerve stimulation". *Acta Neurol Scand.* 2012*;* 126 (5):336-43.

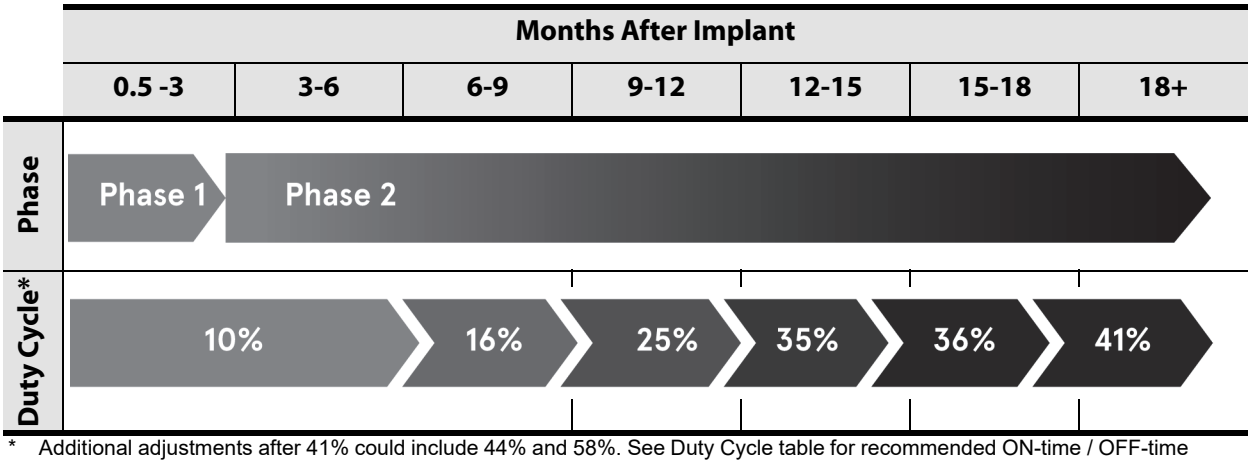
Table 31. Duty Cycle Table of Adjustments

ON Time (sec)	OFF Time (min) 0.2	0.3	0.5	0.8	1.1	1.8	3	5	10
7	58	←44	30	20	15	10	6	4	2
14	69	56	↖41	29	23	15	9	6	3
21	76	64	49	↖36	29	19	12	8	4
30	81	71	57	44	↖35	←25	←16	←10	5
60	89	82	71	59	51	38	27	18	10

For devices with AutoStim enabled, OFF times ≤ 0.8 minutes cannot be used.

Table 32 shows an example of Phase 1 and 2 adjustments over time.

Table 32. Example — Phase 1 and 2 Adjustments Over Time



* Additional adjustments after 41% could include 44% and 58%. See Duty Cycle table for recommended ON-time / OFF-time combinations.

5.2.5 Optimize Generators Capable of AutoStim

5.2.5.1 Optimize the Heartbeat Detection setting

The AutoStim feature relies on accurate heartbeat detection in order to perform as intended. The device performs heartbeat detection by detecting the R-wave of the ECG morphology, which is known to vary based on the posture and body position of the patient. Therefore, a pre-operative assessment of R-wave amplitudes at different body positions is recommended in order to verify minimum detection requirements and to optimize Heartbeat Detection. Instructions for the assessment can be found in the Implantation Procedure chapter. Of the measurements recorded, use the average R-wave amplitude to choose an appropriate Heartbeat Detection setting based on the ranges listed in Table 33.

Table 33. Heartbeat Detection Mapping

Heartbeat Detection	Average Amplitude (mV) (across different postures)	
	Minimum	Maximum
5	0.40	0.50
4	0.51	0.70
3	0.71	0.85
2	0.86	1.25
1	1.26	--

If previous R-wave measurements are not available, either of the following options can be performed as an alternative:

- Repeat the measurements as instructed in the *Implantation Procedure* chapter to determine the average R-wave amplitude.
- Test each of the 5 Heartbeat Detection settings using the Verify Heartbeat Detection feature at each of the 2 body positions and choose the setting that accurately detects heartbeats in both positions.

Note: The Verify Heartbeat Detection feature is described in the programming system physician's manuals.

At subsequent follow-up office visits, the physician should verify that the generator continues to accurately detect the heart rate, and adjust the heartbeat detection setting, if needed.

5.2.5.2 Optimize the AutoStim Threshold setting

The clinician can adjust the sensitivity of the underlying detection algorithm. Six AutoStim Threshold settings are available, 20% - 70% (in 10% increments), each of which correspond to the threshold that the heart rate must surpass in order to elicit a detection (only if detection is enabled) or a detection followed by the triggering of AutoStim (if detection is enabled and AutoStim output current is > 0 mA).

Note: When Detection is "ON", the programming software prevents selection of Normal Mode OFF times less than 1.1 minutes to allow the device sufficient time to detect heart rate changes during each "OFF" cycle.

The objective to optimizing the AutoStim Threshold setting for an individual patient is to reduce the number of detections due to normal, autonomic heart rate changes while maintaining a sensitivity that will detect heart rate changes associated with many seizures.

Clinicians may use a variety of tools to establish a reasonable baseline (e.g., heart rate monitors, Holter monitors, etc.). To assess normal baseline heart rates, the clinician can measure heart rate while the patient is lying down, sitting, or standing (HR_{BL}). After a baseline is established, the clinician can assess a rise in heart rate (HR_{ACT}) during activity by monitoring the heart rate during normal day-to-day activities. The following equation calculates the percent rise from baseline to active (%$HR_{NORM\ INCR}$).

$$(HR_{ACT} - HR_{BL}) / HR_{BL} \times 100 = \%HR_{NORM\ INCR}$$

To determine the heart rate rise during a seizure, the clinician may utilize the electrocardiogram (ECG) collected during the patient's epilepsy monitoring unit (EMU) stay.

Note: See Figure 35 for an illustration of steps 1 and 2.

1. In the electroencephalography (EEG) recording, go to the beginning of a seizure. Scan up to 5 minutes before the electrographic or clinical onset of the seizure and pick a 10-second period of time to establish a baseline heart rate ($HR_{EEG\ BL}$). Within that 10-second window, count the number of R-R intervals and multiply by 6.

$$HR_{EEG\ BL} = (\#\ of\ R\text{-}R\ intervals) \times 6$$

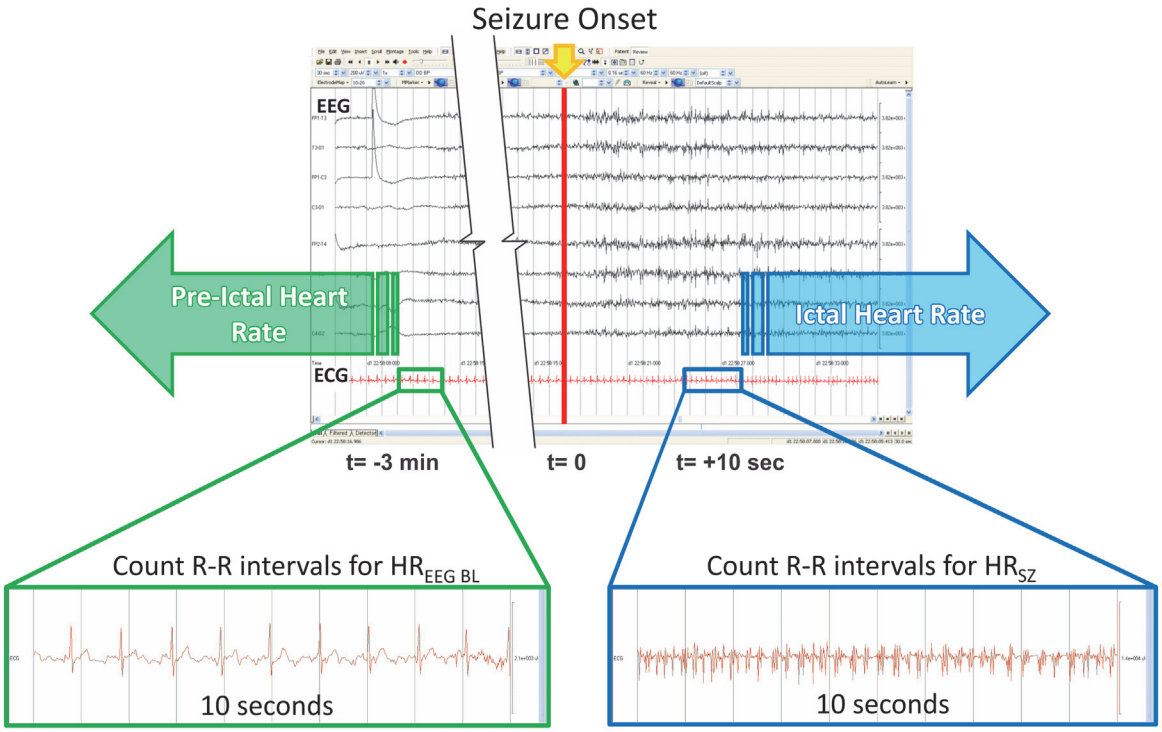
Alternatively, a different section of ECG recording may be used to calculate the pre-ictal heart rate:

- Obtain the simple average heart rate from at least two non-seizure epochs occurring at least 12 hours after or 1 hour prior to a seizure, with the patient in the same state as the start of the seizure.
- Obtain the simple average heart rate from at least two clinical measurements of the patient's heart rate while sitting in the clinic, measured at least 5 minutes apart. These should occur at least 12 hours after or 1 hour prior to a seizure.

2. In the same recording, identify the beginning of the electrographic or clinical onset of the seizure. Scan the seizure and choose a 10-second period of time of maximum heart rate during the seizure (HR_{SZ}). Count the number of R-R intervals and multiply by 6.

$$HR_{SZ} = (\#\ of\ R\text{-}R\ intervals) \times 6$$

Figure 35. Calculation of Baseline Heart Rate and Heart Rate During a Seizure



For this example (Figure 35), the baseline heart rate was assessed by scanning the ECG and finding a 10-second window of time approximately 3 minutes *prior to* seizure onset. Heart rate during the seizure was assessed by finding a 10-second window starting approximately 10 seconds *after* seizure onset.

3. Calculate the percent increase (%$HR_{SZ\ INCR}$) from baseline:

$$(HR_{SZ} - HR_{EEG\ BL}) / HR_{EEG\ BL} \times 100 = \%HR_{SZ\ INCR}$$

If $\%HR_{SZ\ INCR} > \%HR_{NORM\ INCR}$ then choose an AutoStim Threshold setting that represents a threshold between the two values. For example, if $\%HR_{SZ\ INCR}$ is 51% and $\%HR_{NORM\ INCR}$ is 34%, then an AutoStim Threshold setting of 40% or 50% should be chosen. An AutoStim Threshold setting of 50% should be chosen if a lower potential false positive rate is desired or an AutoStim Threshold setting of 40% should be chosen if a higher sensitivity is desired.

If a patient's normal day-to-day heart rate increases are similar to or greater than their increases in heart rate during a seizure, then choose an AutoStim Threshold setting that represents a threshold lower than the $\%HR_{SZ\ INCR}$. For example, if $\%HR_{SZ\ INCR}$ is 62% and $\%HR_{NORM\ INCR}$ is 68%, then an AutoStim Threshold setting of 60% should be chosen. In this scenario the patient may expect to receive additional stimulations. If

bothersome, these stimulations can be inhibited by applying the magnet over the generator for at least 3 seconds.

5.3 Patient Counseling Information

Patients should be told to test their generator's operation daily by performing magnet stimulation and verifying that stimulation occurs. If stimulation does not occur, their physician should be contacted.

It should be noted that the magnet stimulation timing is not synchronized with the timing clock used for determining ON time and has a tolerance of +/- 15% or +/- 7 seconds. Therefore, if the Magnet Mode ON time is programmed to 7 seconds and the generator is swiped at the end of the clock cycle, magnet stimulation may not be perceived by the patient. If the patient does not perceive the magnet stimulation, he or she should be instructed to swipe the generator a second time.

Note: See the "Stimulation" section in the device-specific Technical Information chapter.

In the unlikely event of uncomfortable adverse events, continuous stimulation, or other malfunction, the patient must be advised to hold or tape the magnet directly over the implanted generator to prevent additional stimulation. If patients or caregivers find this procedure necessary, they should immediately notify the patient's physician.

6 Revision / Replacement / Removal Procedure

6.1 Introduction

Revision, replacement, or removal of the VNS Therapy System or any component of the system may be desired for several reasons:

- Replacement of the generator may be required due to pending End-of-Service (EOS) of the generator or if EOS has been reached and the generator cannot communicate or provide therapy.
- Revision/replacement of the lead may be necessary if a broken or damaged lead is suspected, based on diagnostic testing or x-ray evaluation.
- Removal of the VNS Therapy System may be required in cases of infection or for certain medical procedures (e.g., MRI) contraindicated by the labeling (see the *Introduction to the VNS Therapy System* chapter).

Note: Return explanted or opened and unused component(s) of the VNS Therapy System to the company. A Return Product Kit is available from Technical Support.

The following instructions are intended to be general guidelines. If you have questions about the procedures, call Technical Support.

6.2 VNS Therapy Components and Surgical Materials

The following materials should be available before performing a revision of any component of the VNS Therapy System.

6.2.1 Dual-Receptacle Generator Replacement

- Primary and backup dual-receptacle generators
- Two backup single-receptacle generators

6.2.2 Single-Receptacle Generator Replacement

- Primary and backup single-receptacle generators

6.2.3 Other Necessary VNS Therapy Components and Surgical Materials

- Primary and backup single-pin leads

  Note: Revision surgeries involving dual-pin leads require the availability of a new single-pin lead, and both single-receptacle and dual-receptacle generators.

- Tunneler
- Accessory pack
- Programming system
- Sterile laser arm bag or equivalent (not provided by LivaNova)
- Soft vessel loops or silicone sheet (not provided by LivaNova)

6.3 VNS Therapy System Revisions

For all revision surgeries, the patient should consent pre-operatively to receiving a new generator and new lead in case either is damaged during the revision surgery.

6.3.1 Procedure - Replacement of the Generator

6.3.1.1 Pre-operative steps

1. Use the programming system to interrogate the existing generator and perform System Diagnostics (Lead Test) before the patient enters the OR.

   Note: For detailed information about Systems Diagnostics, see "Test the VNS Therapy System" in the *Implantation Procedure* chapter.

2. It is recommended that the surgeon review an x-ray of the generator to determine the routing of the lead. This helps to avoid inadvertent damage to the lead during dissection to remove the generator.
3. If System Diagnostics results indicate "HIGH" or "LOW" lead impedance or the x-ray review shows a gross discontinuity in the lead [lead break or pin(s) disconnected], proceed to "Procedure – Replacement of the VNS Therapy Lead".
4. If System Diagnostics results indicate "OK" lead impedance, use the programming system, outside the sterile field in the OR, to interrogate the replacement generator. This ensures clear communication.

   Note: If the replacement generator is capable of tachycardia detection, the existing generator pocket location may need to be revised.

5. If the replacement generator is capable of tachycardia detection (i.e., Model 106 or 1000/1000-D), verify that the current generator implant location satisfies the requirements outlined in "Determine acceptable device implant locations (tachycardia detection only)" section of the *Implantation Procedure* chapter. If the current implant location does not satisfy the minimum R-wave amplitude requirements, use the same procedure to identify a suitable location close to the original implant site to place the new generator.

   Note: If possible, try to place the replacement generator at rib 4 or above, so the patient can have the maximum flexibility for MRI post-operatively. See MRI with the VNS Therapy System for details.

6. Program the patient data into the new generator.

6.3.1.2 Intra-operative steps

Caution: Do not use electrosurgical equipment after the new generator has been introduced to the sterile field. Exposure to this equipment may damage the generator.

1.With the lead pin(s) still connected, remove the existing generator from the pocket.

2. Open the new generator sales pack. Use the hex screwdriver to disconnect the existing generator from the implanted lead. Remove the lead connector pin(s) from the lead receptacles by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than half a turn should be required to remove the lead.

Caution: When using the hex screwdriver, grasp it by the handle only. Touching the metal shaft while the hex screwdriver is engaged with the setscrew can conduct an electrostatic discharge into the device circuitry and may damage the generator.

Note: Extraneous pocket space left behind from the replacement of a larger generator with a smaller generator may increase the likelihood of certain adverse events (e.g., seroma, device manipulation, and device migration).

Note: Replacement of a smaller generator with a larger generator may require enlargement of the generator pocket during surgery. Physicians should assess the potential impact to post-surgical recovery time and likelihood of temporary patient discomfort due to surgical alteration of the generator pocket.

3. Connect the replacement generator to the lead following the steps in the "Connect the Lead to the Generator" section in the *Implantation Procedure* chapter and complete the remainder of the implantation procedure.

6.3.2 Procedure – Replacement of the VNS Therapy Lead

Note: Consult the prescribing physician before the surgery to determine parameter settings following placement of the new generator.

6.3.2.1 Pre-operative steps

1. Use the programming system to interrogate the existing generator and perform System Diagnostics (Lead Test) before the patient enters the OR. LivaNova recommends that the surgeon review x-rays to confirm the existence of a lead discontinuity [lead break or pin(s) disconnected], if possible.
2. If System Diagnostics results indicate "OK" lead impedance, there is no gross discontinuity in the lead from the x-ray review, and a short-circuit condition is not suspected, the implanted lead is functioning properly. Reassess proceeding with surgery or, if replacement of the generator is still desired, proceed to "Procedure - Replacement of the Generator".
3. If System Diagnostic results indicate "HIGH" or "LOW" lead impedance or a gross lead discontinuity is observed, surgical intervention is required. Use the programming system, outside the sterile field in the OR, to interrogate all potential replacement generators. This ensures clear device communication.
4. If the replacement generator is capable of tachycardia detection (i.e., Model 106 or 1000/1000-D), verify that the current generator implant location satisfies the requirements outlined in "Determine acceptable device implant locations (tachycardia detection only)" section of the *Implantation Procedure* chapter. If the current implant location does not satisfy the minimum R-wave amplitude requirements, use the same procedure to identify a suitable location close to the original implant site to place the new generator.
5. Proceed to "Intra-operative steps" below.

6.3.2.2 Intra-operative steps

Note: For complete troubleshooting steps, see "Troubleshooting" in the programming system physician's manuals.

6.3.2.2.1. "HIGH" lead impedance on System Diagnostics

If "HIGH" lead impedance is reported, perform the following steps:

1. With lead pin(s) still connected, remove the existing generator from the pocket.
2. Open the accessory pack and remove the hex screwdriver and test resistor.
3. Remove the lead connector pin(s) from the lead receptacle(s) by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than a half turn should be required to remove the lead.
4. If foreign material (e.g., blood) is observed in the generator receptacle(s), flush the receptacle(s) with saline to remove the foreign material. Drain the excess fluid from the receptacle(s). Do not place any object (other than the connector pin) into the receptacle. Use saline to clean the lead connector pin(s), then wipe dry.
5. Re-insert the existing lead connector pin(s) into the existing generator following proper lead insertion techniques.

   Note: For proper lead insertion techniques, see "Connect the Lead to the Generator" in the *Implantation Procedure* chapter.

   Caution: Visually inspect that the connector pin(s) is clean and completely inserted.
6. Introduce the programming system into the sterile field with a sterile laser arm bag (or equivalent) and perform an interrogation followed by System Diagnostics.
7. Record System Diagnostics results.

   - If the results indicate "OK" lead impedance, the previous "HIGH" lead impedance was resolved and the system appears to be functioning properly. Assess replacement of the generator.

     If replacement of the generator is not desired, verify that all relevant steps outlined in "Test the VNS Therapy System" section of the *Implantation Procedure* chapter have been completed. Finish the procedure by following the steps in "Complete the Implantation Procedure" section in the *Implantation Procedure* chapter.

     If replacement of the generator is desired, open a new compatible generator sales pack. Connect the replacement generator to the lead following the steps in the "Connect the Lead to the Generator" section in the *Implantation Procedure* chapter and complete the remainder of the implantation procedure. Ensure appropriate patient data has been programmed into the new generator.

     Note: The prescribing physician will program the stimulation parameters post-operatively based on the patient's tolerance to the stimulation.

   - If System Diagnostics results continue to report "HIGH" lead impedance, perform Generator Diagnostics (Pre-Implant Test) with the test resistor assembly from the accessory pack to verify that the generator is functioning properly, independent of the lead. To perform Generator Diagnostics, follow the steps in "Generator Diagnostics (Pre-Implant Test)" below.

6.3.2.2.2. "LOW" lead impedance on System Diagnostics

Note: For complete troubleshooting steps see "Troubleshooting" in the programming system physician's manuals.

If System Diagnostics report "LOW" lead impedance, perform Generator Diagnostics (Pre-Implant Test) with the test resistor assembly from the accessory pack to verify that the generator is functioning properly, independent of the lead.

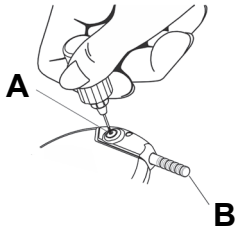
To perform Generator Diagnostics (Pre-Implant Test), follow the steps in "Generator Diagnostics (Pre-Implant Test)" below.

6.3.2.3 Generator Diagnostics (Pre-Implant Test)

1. Insert the connector pin(s) of the resistor assembly into the lead receptacle(s). Be careful while inserting the test resistor pin(s) into the lead receptacle(s). If binding or significant resistance is felt, remove the test resistor, inspect it, and clean it if necessary. Without the use of excessive force, reinsert the test resistor.
2. When the resistor assembly is in place, tighten the setscrew(s) until the hex screwdriver begins to click (see Figure 36). Always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

Figure 36. Connect the Resistor Assembly

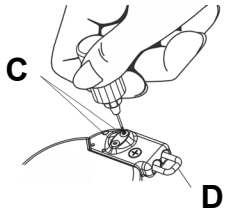
Single-Receptacle Generator



A Setscrew Plug

B Resistor Assembly

Dual-Receptacle Generator



C Setscrew Plugs (2)

D Resistor Assembly

3. Perform Generator Diagnostics (Pre-Implant Test).

   Note: For details, see the programming system physician's manuals.

   - If Generator Diagnostics results indicate "HIGH" or "LOW" lead impedance, call Technical Support.
   - If Generator Diagnostics results indicate "OK" lead impedance, the implanted lead should be replaced and Generator replacement assessed.

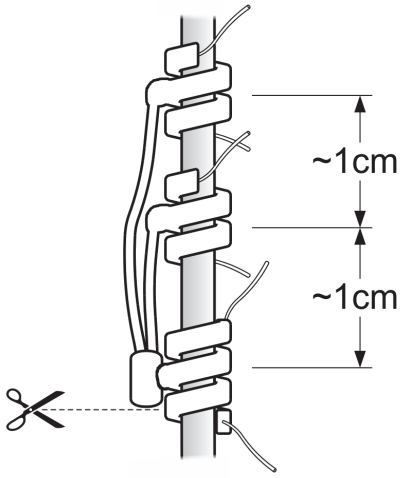
6.3.2.4 Remove existing helices and lead

Caution: Lead replacement or removal is a medical judgment that must be carefully weighed against the known and unknown risks of surgery. At present there are no known long-term hazards or risks associated with leaving the lead implanted, beyond those mentioned in this physician's manual.

1. Open the neck incision and locate the vagus nerve/helices interface.
2. Assess the degree of fibrotic encapsulation to determine if the entire lead can be removed safely.
   - If removal of the existing helices can be accomplished, the new helices may be placed in the same location.
   - If complete removal of the helices from the nerve is not possible, transect as much of the lead as possible. With ≤ 2 cm of the lead remaining (see Figure 37) a full body MRI using the body coil to transmit RF is allowable. (See the *MRI with the VNS Therapy System* chapter for further details.).

- If it is not possible to leave ≤ 2 cm, then MRI can still be performed for brain or extremity imaging with the appropriate type of T/R coil. (See *MRI with the VNS Therapy System* chapter for further details.)

Figure 37. Transected Lead (≤ 2 cm)



3. The replacement helices can be placed above or below the existing helices if they must remain.

6.3.2.5 Complete the procedure

Complete the remainder of the implant procedure per the *Implantation Procedure* chapter, starting with the steps in the "Implant the lead" section. Pay particular attention to all cautions and warnings regarding the cardiac branches.

Note: The prescribing physician will program the stimulation parameters post-operatively after the recommended 2-week recovery period to allow the nerve to heal.

6.4 Removal of the VNS Therapy System

If removal is medically necessary, LivaNova recommends removing as much of the VNS Therapy System as can be safely accomplished:

- Assess the degree of fibrotic in-growth in and around the helices.
- Remove the entire system, if possible.
- If fibrotic encapsulation hinders safe removal of the entire system, transect as much of the lead wire as possible (see Figure 37).
- Removal of the generator alone does not alter the hazards associated with certain MRI procedures.

  Note: For detailed information, see the *MRI with the VNS Therapy System* chapter.

- Diathermy procedures are contraindicated for patients with any portion of the VNS Therapy System remaining in the body.

  Note: For detailed information regarding the use of diathermy with VNS, see the *Introduction to the VNS Therapy System* chapter.

7 Troubleshooting

7.1 Model 102 and 102R

7.1.1 "Patient Cannot Feel Stimulation" at Follow-up Visit (Models 102-102R)

A patient may not feel stimulation if any of the following situations exist:

- Patient has become accustomed to the programmed setting
- Device is approaching its end of service (EOS)
- "High" lead impedance
- Short-circuit condition within the lead
- Generator issue

To determine the cause of the situation, perform the following steps:

1. Swipe the magnet. Ask the patient if they feel the magnet activation, experience any voice alteration, or experience any other common side effect to indicate the presence of stimulation.

   Note: Ensure that the technique for swiping the magnet over the device is correct according to the section "Initiating stimulation with a magnet" in the102/102R Technical Information chapter. Also see "Potential Adverse Events" in the indication-specific information chapters for a complete list of possible adverse events.

2. Interrogate the generator.
3. Perform a System Diagnostics (Lead Test) and record the results.

IF…	*THEN…*
Model 250 version 11.0 software and below: If the DC-DC Converter Code is "0" or there has been a significant decrease in DC-DC Converter Code value (e.g., "3" to "1") in respect to prior System Diagnostics **Model 3000 version 1.0 software and above:** If the impedance is ≤ 1700 Ohms or if there has been a sudden change in impedance range (e.g., 4100-5200 Ohms to 1800-2800) in respect to prior System Diagnostics	A short-circuit condition may be present within the lead and the patient may not be receiving the intended therapy. For more information, see "Short-circuit conditions within the lead" in the *102/102R Technical Information* chapter.
Model 250 version 11.0 software and below: If the DC-DC Converter Code is not "0", there has been no significant decrease in DC-DC Converter Code value (e.g., "3" to "1") in respect to prior System Diagnostics, and the System Diagnostics test indicates the lead impedance is "OK" **Model 3000 version 1.0 software and above:** If System Diagnostics test indicates the lead impedance is OK	The system is functioning properly and the patient could have become accustomed to the settings, as do many patients.
If the System Diagnostics test indicates the lead impedance is "High"	See "Troubleshooting" in the programming system physician's manuals.

Caution: For the System Diagnostics (Lead Test), the software automatically programs the generator to 1 mA, 500 µsec, and 20 Hz. Patients whose generator output current is normally *less* than these values may experience increased sensation, coughing, a flushed face, or other effects. For a complete list of possible adverse events, see "Potential Adverse Events" in the indication-specific information chapters.

4. Perform a Normal Mode Diagnostics test and record the results.

IF…	*THEN…*
The Normal Mode Diagnostics test indicates the Output Current is "LIMIT"	The generator cannot deliver programmed output. Consider reducing output current or frequency and widening the pulse width.
The Normal Mode Diagnostics test indicates the Output Current is "OK"	The generator can deliver the programmed output current. **Note**: To obtain accurate information from the device diagnostics, the generator must be programmed to a **minimum** of 0.75 mA, 15 Hz, and **at least** 30 seconds ON time.
The Normal Mode Diagnostics test indicates "HIGH" lead impedance	See "Troubleshooting" in the programming system physician's manuals.

5. If further assistance is needed, call Technical Support.

7.1.2 Magnet Activation Not Working at Follow-up Visit (Models 102-102R)

A patient's magnet activation may not be working if any of the following situations exist:

- Patient may have become accustomed to the programmed setting.
- An incorrect technique is used for swiping the magnet.
- Magnet output current is not programmed to ON.
- Device is approaching its end of service (EOS).
- Device was implanted too deep.
- There is an issue with the generator.
- "High" lead impedance
- Short-circuit condition within the lead

To determine the cause of the situation, perform the following steps:

1. Interrogate the device.
2. Confirm that the Magnet Output Current is ≥ 0.25 mA and Magnet ON time is > 7 seconds.
3. Record the number of magnet activations listed under Device History or Events screen of the programming software.
4. Swipe the magnet over the device and watch for a clinical response to the stimulation. Wait 3 to 4 minutes and re-interrogate the device.

Note: Ensure that the technique for swiping the magnet over the device is correct according to the section "Initiating stimulation with a magnet" *102/102R Technical Information* chapter.

Note: Follow the listed instructions and swipe the magnet just before starting the test. To obtain accurate information from the device diagnostics, the generator must be programmed to a **minimum** of 0.75 mA (Magnet Output Current), 15 Hz (Normal Mode Frequency), and 30 seconds (Magnet ON Time).

5. Record the number of magnet activations again. The number of activations should have increased by 1.

6. If the number of magnet activations increased but the patient does not feel magnet-induced stimulation, increase the magnet output current until the magnet-induced stimulation is felt.
7. If the number of magnet activations did not increase, perform a Magnet Mode Diagnostics test and record all results.

IF…	***THEN…***
The Magnet Mode Diagnostics test indicates OK results	The magnet is functioning properly and the patient could have become accustomed to the settings, as do many patients.
The Magnet Mode Diagnostics test indicates device status "STANDBY" and output current "****", or gives a message that the magnet swipe was not detected	Perform steps 1 through 7 with an alternate VNS Therapy magnet.
The Magnet Mode Diagnostics test indicates "HIGH" lead impedance	See "Troubleshooting" in the programming system physician's manuals.

8. If further assistance is needed, call Technical Support.

7.2 Model 103, 104, 105 106, and 1000/1000-D

7.2.1 "Patient Cannot Feel Stimulation" at Follow-up Visit (Models 103-106 and 1000/1000-D)

A patient may not feel stimulation under any of these conditions:

- Patient has become accustomed to the programmed setting
- Generator battery at end of service (EOS)
- "High" lead impedance
- Defective generator
- Disabled generator
- Short-circuit condition within the lead

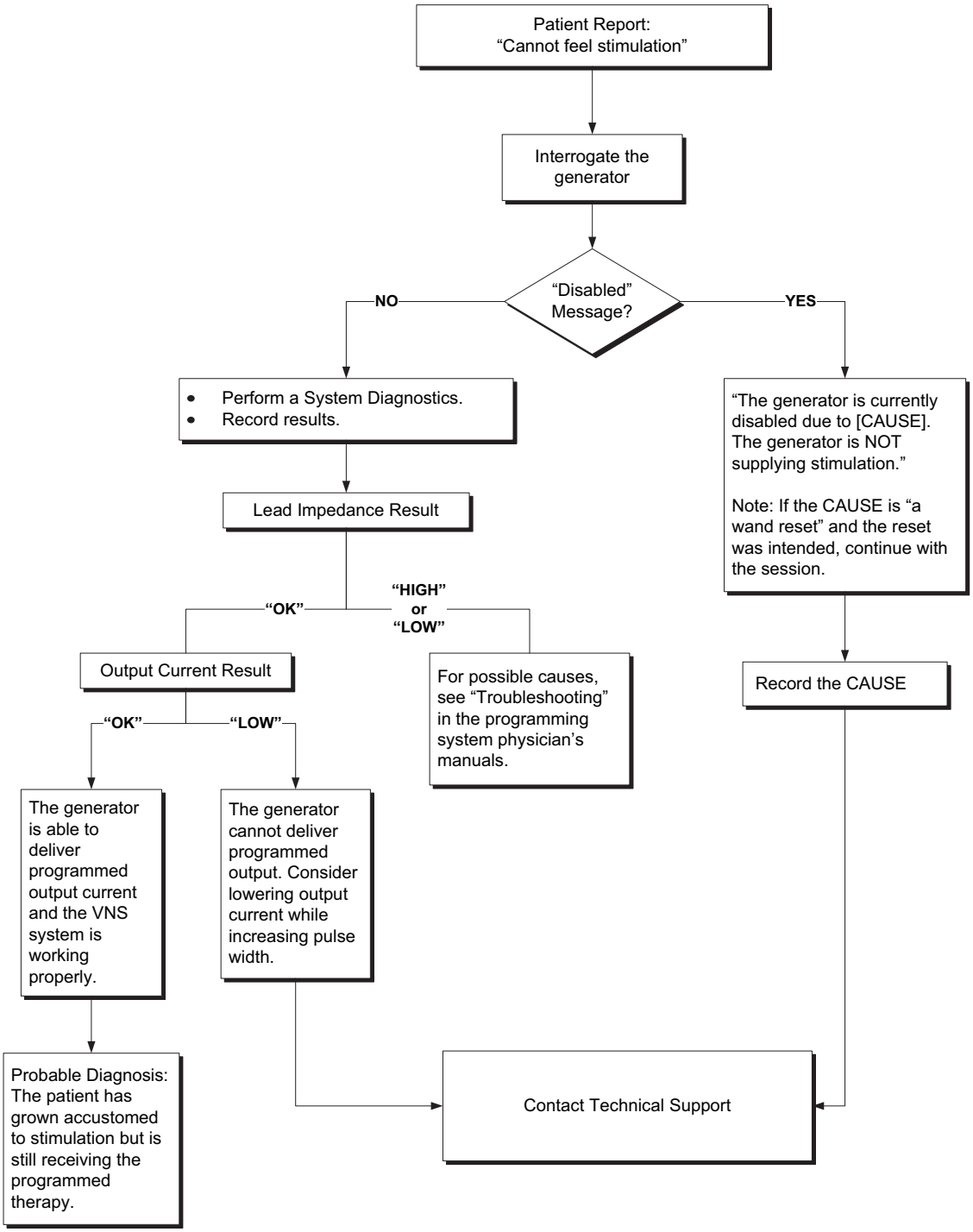
To determine the cause of the condition, perform these steps (see Figure 38):

1. Interrogate the generator.
   - If the following message appears, call Technical Support: "The generator is currently disabled due to [CAUSE]. The generator is NOT supplying stimulation."

     Note: If the CAUSE is "a wand reset" and the reset was intended, continue with the session.

2. Perform a System Diagnostics and record the results.
   - If the output current reports "OK" and lead impedance reports "OK," then the generator is able to deliver the programmed therapy and the patient may have become accustomed to the stimulation, as do many patients.
   - If the output current reports "OK" and lead impedance reports "LOW" (≤ 600 Ohms), then there is a possibility of a short-circuit condition within the lead. See "Troubleshooting" in the programming system physician's manuals.
   - If the output current reports "LOW" and lead impedance reports "OK," then the generator cannot deliver programmed output due to increased impedance. Consider lowering the output current while increasing pulse width.
   - If the output current reports "LOW" and lead impedance reports "HIGH" (≥ 5300 Ohms), see "Troubleshooting" in the programming system physician's manuals.
3. For further assistance, call Technical Support.

Figure 38. "Patient Cannot Feel Stimulation" at Follow-Up Visit (Models 103-106 and 1000/1000-D)



7.2.2 "Patient Cannot Feel Magnet Activation" at Follow-up Visit (Models 103-106 and 1000/1000-D)

Magnet activation may not be perceived under any of these conditions:

- Patient has become accustomed to the programmed setting
- Incorrect technique for swiping magnet
- Magnet output current is programmed to 0 mA
- Generator battery at end of service (EOS)
- Device implanted too deep in the chest
- Defective generator
- Disabled generator
- "High" lead impedance
- Short-circuit condition within the lead

To determine the cause of the condition, perform these steps (see Figure 39):

1. Interrogate the device.
   - If the following message appears, call Technical Support: "The generator is currently disabled due to [CAUSE]. The generator is NOT supplying stimulation."

     Note: If the CAUSE is "a wand reset" and the reset was intended, continue with the session.
2. Confirm that the magnet output current is ≥ the Normal output current and magnet ON time is >7 seconds.
3. Record the number of magnet activations listed on the Device History or Events screen of the programming software.
4. Swipe the magnet over the device.

   Note: Ensure that the technique for swiping the magnet over the device is correct. (See "VNS Therapy magnets" in the *Technical Information - VNS Therapy Generators* chapter.)

   The number of magnet activations may increase by 1 or 2 with the cross-pattern swipe technique.
5. Reinterrogate the device.
6. Check the number of magnet activations again. The number of magnet activations should have increased.

- If the number of magnet activations increased, the generator is delivering the magnet stimulation. Consider raising the magnet current if perceived stimulation is desired.

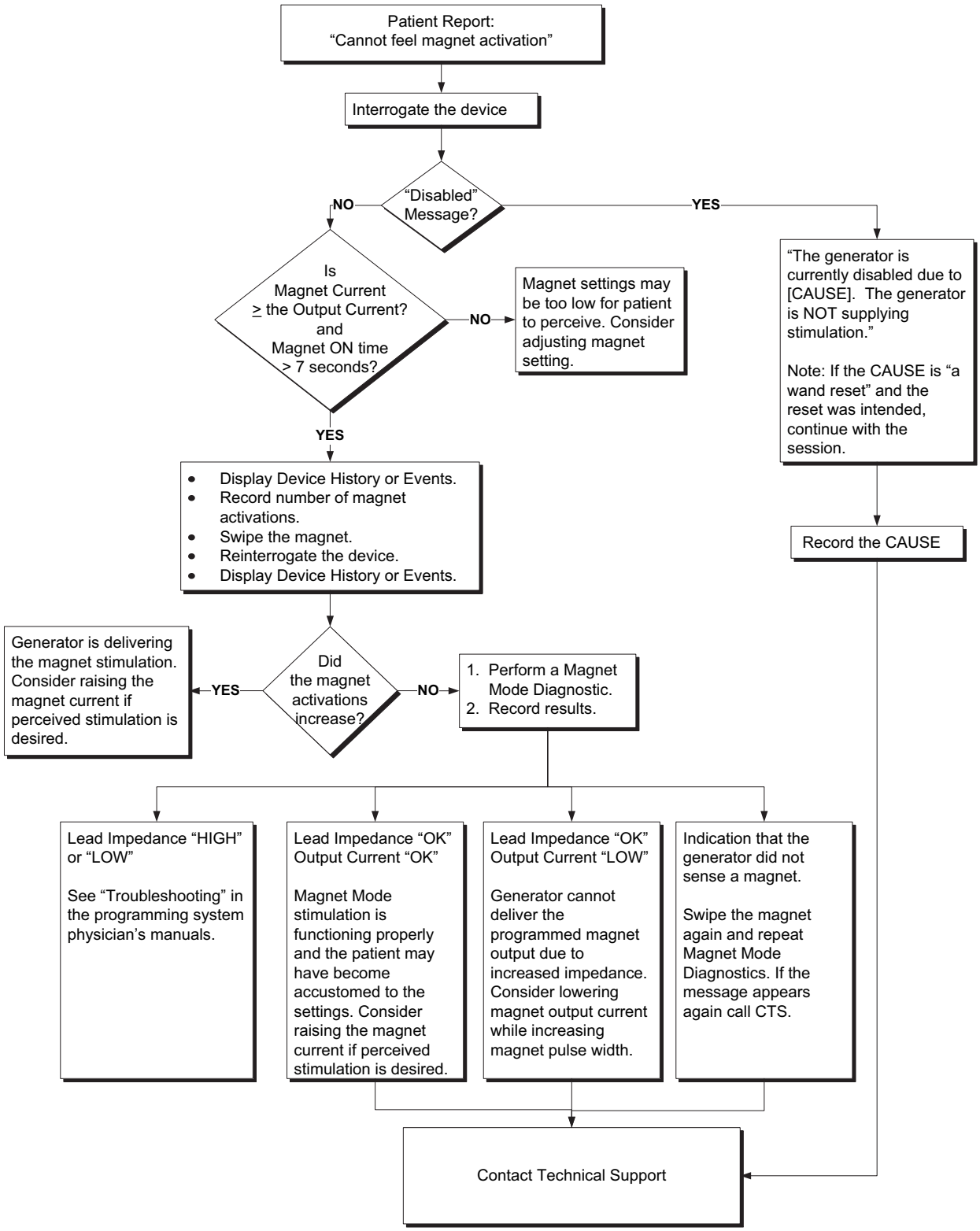
- If the number of magnet activations did not increase with the test swipe, perform a Magnet Mode Diagnostics. Record all results.
    - If the generator did not sense a magnet swipe, then you will see an indication that the generator did not sense a magnet. Swipe the magnet again and repeat Magnet Mode Diagnostics. If the warning appears again, call Technical Support.

      Note: Follow the listed instructions and swipe the magnet just before starting the test.

    - If the output current reports "OK" and lead impedance reports "OK," then the Magnet Mode stimulation is functioning properly and the patient may have become accustomed to the settings.
    - If the output current reports "LOW" and lead impedance reports "OK," then the generator cannot deliver the programmed magnet output due to increased impedance. Consider lowering the magnet output current while increasing the magnet pulse width.
    - If the output current reports "LOW" and lead impedance reports "HIGH," see "Troubleshooting" in the programming system physician's manuals.

7. For further assistance, call Technical Support.

Figure 39. "Patient Cannot Feel Magnet Activation" at Follow-Up Visit (Models 103-106 and 1000/1000-D)



7.2.3 "Patient Does Not Perceive AutoStim Activation" at Follow-up (Generators with AutoStim only)

AutoStim activation may not be perceived under any of these conditions:

- AutoStim Threshold is too high (e.g., 70% threshold versus 50%)
- Patient has become accustomed to the programmed setting
- AutoStim output current is programmed to 0 mA
- Generator battery at end of service (EOS)
- Defective generator or lead
- Disabled generator

If AutoStim activation is not perceived, perform these steps (see Figure 40):

1. Ensure the programming computer is unplugged and Interrogate the device.
   - If the following message appears, call Technical Support: "The generator is currently disabled due to [CAUSE]. The generator is NOT supplying stimulation."

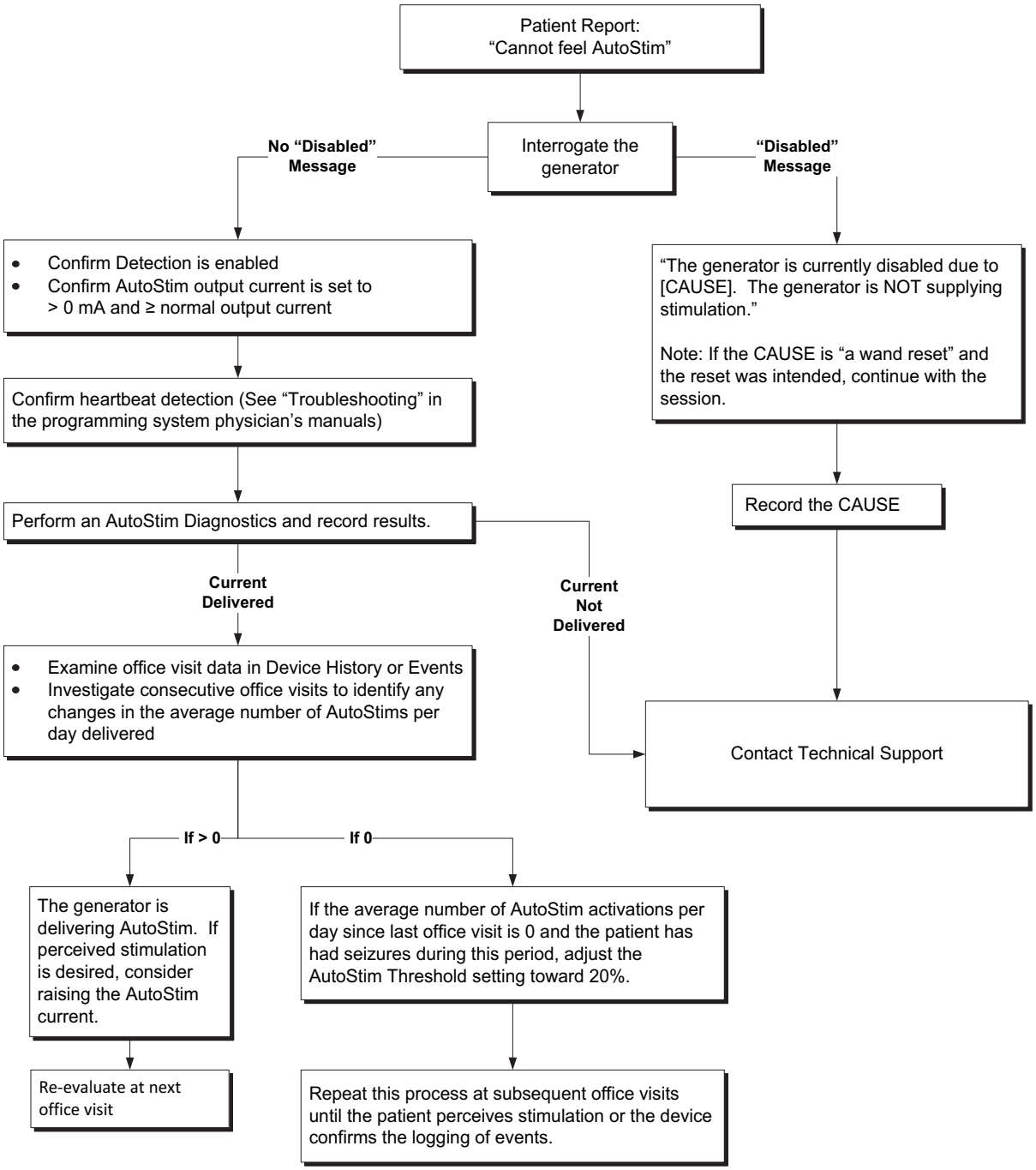
     Note: If the CAUSE is "a wand reset" and the reset was intended, continue with the session.

2. Confirm that Detection is enabled and the AutoStim output current is set to a value > 0 mA and ≥ the Normal output current.
3. Confirm heartbeat detection (See "Troubleshooting" in the programming system physician's manuals)
4. Perform AutoStim Diagnostics from the Device Diagnostics Menu.
   - If the diagnostics indicates that the AutoStim output current was delivered, re-evaluate at the next office visit.
5. Look at the Office Visit data under Device History or Events and investigate consecutive office visits to identify any changes in the average number of AutoStims per day delivered by the device.
6. Make note of the average number of AutoStims per day since the last visit.
   - If the average number of AutoStim per day is > 0, the generator is delivering the AutoStim stimulation as detected by the algorithm. Consider raising the AutoStim current if perceived stimulation is desired.
   - If the average number of AutoStim activations per day since last office visit is 0 and the patient has had seizures during this period, adjust the AutoStim Threshold toward 20%. Repeat this process at subsequent office visits until the patient perceives stimulation or the device confirms the logging of events.

     Note: Decreasing the detection threshold increases the likelihood of detecting heart rate rises associated with seizures, but may increase the overall number of AutoStims delivered and impact battery longevity. See *Technical Information - VNS Therapy Generators* chapter for additional information.

7. For further assistance, call Technical Support.

Figure 40. "Patient Does Not Perceive AutoStim Activation" at Follow-up (Generators with AutoStim Only)



8 Limited Replacement Warranty

LivaNova USA, Inc. warrants the VNS Therapy generator and lead against any defects due to faulty material or workmanship for a period of two (2) years from the date of implantation. This warranty applies only to the original purchaser of the VNS Therapy generator and lead and the patient implanted with it. This Limited Replacement Warranty also applies only when the product is used in accordance with the product's physician's manual and excludes damage due to improper handling, defacing, accident (including dropping), or misuse. This product is not warranted when used or implanted by a person(s) not trained in or familiar with the VNS Therapy System and Programming System physician's manuals. This Limited Replacement Warranty is not a representation that any one VNS Therapy generator or lead will last the entire time of the Limited Replacement Warranty.

In no event shall LivaNova USA, Inc. be liable for any special, incidental, indirect, or consequential damages based on the failure of the device to function within normal tolerances, or resulting from damage to the device by external forces, whether the claim is based on warranty, contract, tort, or otherwise, or in connection with the purchase, use, or surgical implantation of this device or associated components or costs over and above the original purchase price from LivaNova USA, Inc.

To qualify for the Limited Replacement Warranty, the following conditions must be met:

1. A properly completed Implant and Warranty Registration form for both the VNS Therapy generator and the VNS Therapy lead must be returned to LivaNova USA, Inc. within sixty (60) days of device implantation;
2. The battery in the VNS Therapy generator cannot have been depleted as a result of programming to unusually high output currents, pulse widths, or duty cycles, which will cause a high energy/current drain;
3. The VNS Therapy lead cannot have been cut or damaged due to excessive handling or abuse during surgical implantation;
4. The product must have been used and prescribed in accordance with the VNS Therapy System and Programming System physician's manuals;
5. The VNS Therapy generator or lead must have been implanted prior to its "Expiration Date;"
6. The defective VNS Therapy generator or lead must be returned to LivaNova USA, Inc. with an accompanying Authorization number, available from Technical Support at 1 (866) 882-8804 (U.S. and Canada) or +1 (281) 228-7330 (Worldwide), and confirmed defective by the Quality Assurance Department; and
7. All returned VNS Therapy generators and leads shall become the property of LivaNova USA, Inc.

> ⚠ **Caution: Return explanted generators and leads** to LivaNova USA, Inc. for examination and proper disposal, along with a completed Returned Product Report form. Before returning the lead, disinfect the device components with Betadine®, Cidex® soak, or another similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

If the VNS Therapy generator or lead becomes defective within the warranty period, contact LivaNova USA, Inc. Customer Service for a no-cost replacement. LivaNova USA, Inc. reserves the right to replace a defective product with the most comparable product currently available.

Returned biohazardous product should be clearly identified as such on the outside surface of the package.

No implied warranty, including, but not limited to, any implied warranty of merchantability or fitness for a particular purpose, shall extend beyond the period specified above. This replacement warranty shall be the exclusive remedy available to any person. No person has any authority to bind LivaNova USA, Inc. to any representation, condition, or warranty except this Limited Replacement Warranty.

While this warranty gives you specific legal rights, you may also have other rights that vary from state to state or that encroach upon the above.

9 Appendices

9.1 Appendix A - Model 102/102R Battery Longevity and Programmed Setting Choices

9.1.1 Nominal Longevity Estimates from Beginning of Life (BOL) to End of Service (EOS)

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	15.3	11.3	9.5
1	10	130	3	15.1	11.1	9.2
1	10	130	5	14.8	10.5	8.7
1	10	130	7	14.4	9.8	8.0
1	10	500	2	14.2	9.6	7.7
1	10	500	3	13.8	8.9	7.1
1	10	500	5	13.0	7.9	6.1
1	10	500	7	12.4	7.3	5.6
1	10	1000	2	12.8	7.6	5.9
1	10	1000	3	12.2	6.9	5.3
1	10	1000	5	10.9	5.7	4.2
1	10	1000	7	10.3	5.2	3.8
1	20	130	2	14.2	9.5	7.6
1	20	130	3	13.8	9.0	7.2
1	20	130	5	13.4	8.5	6.7
1	20	130	7	12.7	7.6	5.9
1	20	500	2	12.3	7.1	5.4
1	20	500	3	11.7	6.5	4.9
1	20	500	5	10.6	5.5	4.0
1	20	500	7	10.0	4.9	3.6
1	20	1000	2	10.3	5.2	3.8
1	20	1000	3	9.6	4.6	3.3
1	20	1000	5	8.2	3.6	2.6
1	20	1000	7	7.5	3.2	2.3
1	30	130	2	13.1	8.1	6.3
1	30	130	3	12.7	7.6	5.9
1	30	130	5	12.2	7.0	5.3
1	30	130	7	11.4	6.2	4.6
1	30	500	2	10.9	5.7	4.2
1	30	500	3	10.2	5.1	3.7
1	30	500	5	9.0	4.2	3.0
1	30	500	7	8.3	3.7	2.6
1	30	1000	2	8.7	3.9	2.8

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	30	1000	3	7.9	3.5	2.4
1	30	1000	5	6.6	2.7	1.8
1	30	1000	7	5.9	2.3	1.6
1.5	10	130	2	14.7	10.3	8.4
1.5	10	130	3	14.4	9.8	7.9
1.5	10	130	5	13.7	8.8	7.0
1.5	10	130	7	13.8	8.9	7.1
1.5	10	500	2	12.4	7.3	5.6
1.5	10	500	3	12.0	6.7	5.1
1.5	10	500	5	10.9	5.7	4.3
1.5	10	500	7	11.2	6.0	4.5
1.5	10	1000	2	10.3	5.2	3.8
1.5	10	1000	3	9.6	4.6	3.3
1.5	10	1000	5	8.4	3.8	2.7
1.5	10	1000	7	8.9	4.1	2.9
1.5	20	130	2	13.1	8.0	6.2
1.5	20	130	3	12.6	7.5	5.8
1.5	20	130	5	11.8	6.5	4.9
1.5	20	130	7	11.8	6.6	5.0
1.5	20	500	2	10.0	5.0	3.6
1.5	20	500	3	9.4	4.5	3.2
1.5	20	500	5	8.2	3.7	2.6
1.5	20	500	7	8.6	3.9	2.8
1.5	20	1000	2	7.5	3.2	2.2
1.5	20	1000	3	6.8	2.8	2.0
1.5	20	1000	5	5.7	2.2	1.5
1.5	20	1000	7	6.2	2.4	1.7
1.5	30	130	2	11.8	6.5	4.9
1.5	30	130	3	11.3	6.1	4.5
1.5	30	130	5	10.3	5.2	3.8
1.5	30	130	7	10.4	5.3	3.9
1.5	30	500	2	8.4	3.8	2.7
1.5	30	500	3	7.7	3.3	2.4
1.5	30	500	5	6.6	2.7	1.9
1.5	30	500	7	7.0	2.9	2.0
1.5	30	1000	2	5.9	2.3	1.6
1.5	30	1000	3	5.3	2.0	1.4
1.5	30	1000	5	4.3	1.6	1.1
1.5	30	1000	7	4.7	1.8	1.2
2	10	130	2	14.1	9.4	7.5
2	10	130	3	13.5	8.5	6.7

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	130	5	13.5	8.5	6.7
2	10	130	7	13.7	8.8	7.0
2	10	500	2	11.2	6.0	4.4
2	10	500	3	10.1	5.0	3.6
2	10	500	5	10.5	5.4	3.9
2	10	500	7	11.1	5.9	4.3
2	10	1000	2	8.4	3.8	2.7
2	10	1000	3	7.4	3.1	2.2
2	10	1000	5	7.9	3.5	2.4
2	10	1000	7	8.6	3.9	2.8
2	20	130	2	12.2	7.0	5.3
2	20	130	3	11.3	6.0	4.5
2	20	130	5	11.4	6.2	4.6
2	20	130	7	11.7	6.5	4.9
2	20	500	2	8.4	3.8	2.7
2	20	500	3	7.3	3.1	2.2
2	20	500	5	7.8	3.4	2.4
2	20	500	7	8.4	3.8	2.7
2	20	1000	2	5.5	2.1	1.5
2	20	1000	3	4.8	1.8	1.2
2	20	1000	5	5.3	2.0	1.4
2	20	1000	7	5.9	2.3	1.6
2	30	130	2	10.8	5.6	4.1
2	30	130	3	9.7	4.7	3.4
2	30	130	5	9.9	4.9	3.5
2	30	130	7	10.2	5.1	3.8
2	30	500	2	6.8	2.8	1.9
2	30	500	3	5.7	2.2	1.5
2	30	500	5	6.2	2.5	1.7
2	30	500	7	6.8	2.8	1.9
2	30	1000	2	4.0	1.4	1.0
2	30	1000	3	3.6	1.3	0.8
2	30	1000	5	4.0	1.4	1.0
2	30	1000	7	4.6	1.7	1.1
3.5	10	130	2	12.6	7.5	5.7
3.5	10	130	3	12.9	7.8	6.0
3.5	10	130	5	13.3	8.3	6.5
3.5	10	130	7	13.5	8.6	6.8
3.5	10	500	2	8.6	3.9	2.8
3.5	10	500	3	9.2	4.4	3.1
3.5	10	500	5	10.1	5.0	3.7

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	10	500	7	10.8	5.6	4.1
3.5	10	1000	2	5.8	2.3	1.6
3.5	10	1000	3	6.5	2.6	1.8
3.5	10	1000	5	7.5	3.2	2.3
3.5	10	1000	7	8.3	3.7	2.6
3.5	20	130	2	10.2	5.1	3.8
3.5	20	130	3	10.6	5.5	4.0
3.5	20	130	5	11.1	5.9	4.4
3.5	20	130	7	11.5	6.3	4.7
3.5	20	500	2	5.9	2.3	1.6
3.5	20	500	3	6.5	2.6	1.8
3.5	20	500	5	7.4	3.1	2.2
3.5	20	500	7	8.1	3.5	2.5
3.5	20	1000	2	3.6	1.3	0.9
3.5	20	1000	3	4.1	1.5	1.0
3.5	20	1000	5	5.0	1.9	1.3
3.5	20	1000	7	5.6	2.2	1.5
3.5	30	130	2	8.6	3.9	2.8
3.5	30	130	3	9.0	4.2	3.0
3.5	30	130	5	9.6	4.6	3.3
3.5	30	130	7	10.0	4.9	3.6
3.5	30	500	2	4.5	1.7	1.1
3.5	30	500	3	5.0	1.9	1.3
3.5	30	500	5	5.8	2.3	1.6
3.5	30	500	7	6.5	2.6	1.8
3.5	30	1000	2	2.7	0.9	0.6
3.5	30	1000	3	3.0	1.0	0.7
3.5	30	1000	5	3.7	1.3	0.9
3.5	30	1000	7	4.3	1.6	1.1

9.1.2 Worst Case Longevity Estimates from Beginning of Life (BOL) to Near End of Service (N EOS)

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	9.3	7.1	6.0
1	10	130	3	9.3	7.2	6.1
1	10	130	5	8.8	6.2	5.1
1	10	130	7	8.8	6.2	5.0
1	10	500	2	9.1	6.8	5.7
1	10	500	3	8.9	6.4	5.2
1	10	500	5	8.2	5.3	4.2
1	10	500	7	8.0	5.0	3.9
1	10	1000	2	8.3	5.4	4.3
1	10	1000	3	8.0	5.1	4.0
1	10	1000	5	7.2	4.1	3.1
1	10	1000	7	6.8	3.7	2.8
1	20	130	2	9.1	6.7	5.6
1	20	130	3	8.9	6.4	5.3
1	20	130	5	8.6	5.9	4.8
1	20	130	7	8.2	5.3	4.2
1	20	500	2	8.2	5.2	4.2
1	20	500	3	7.8	4.8	3.7
1	20	500	5	6.9	3.8	2.8
1	20	500	7	6.7	3.6	2.7
1	20	1000	2	6.9	3.7	2.8
1	20	1000	3	6.6	3.5	2.6
1	20	1000	5	5.7	2.8	2.0
1	20	1000	7	5.2	2.4	1.7
1	30	130	2	8.6	5.9	4.7
1	30	130	3	8.4	5.6	4.4
1	30	130	5	8.0	5.0	3.9
1	30	130	7	7.5	4.5	3.4
1	30	500	2	7.4	4.3	3.3
1	30	500	3	7.0	3.9	2.9
1	30	500	5	6.1	3.0	2.2
1	30	500	7	5.7	2.8	2.0
1	30	1000	2	5.8	2.8	2.0
1	30	1000	3	5.6	2.7	1.9
1	30	1000	5	4.7	2.1	1.5
1	30	1000	7	4.1	1.7	1.2
1.5	10	130	2	9.2	6.9	5.9
1.5	10	130	3	8.9	6.5	5.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	5	8.3	5.4	4.3
1.5	10	130	7	8.3	5.5	4.4
1.5	10	500	2	7.9	4.9	3.8
1.5	10	500	3	7.8	4.8	3.7
1.5	10	500	5	7.1	4.0	3.0
1.5	10	500	7	7.2	4.1	3.1
1.5	10	1000	2	7.0	3.9	2.9
1.5	10	1000	3	6.6	3.5	2.6
1.5	10	1000	5	5.8	2.8	2.0
1.5	10	1000	7	6.0	3.0	2.2
1.5	20	130	2	8.5	5.7	4.6
1.5	20	130	3	8.2	5.3	4.2
1.5	20	130	5	7.6	4.5	3.5
1.5	20	130	7	7.6	4.6	3.5
1.5	20	500	2	6.9	3.8	2.8
1.5	20	500	3	6.5	3.4	2.5
1.5	20	500	5	5.7	2.7	2.0
1.5	20	500	7	5.9	2.9	2.1
1.5	20	1000	2	5.3	2.5	1.8
1.5	20	1000	3	4.9	2.2	1.5
1.5	20	1000	5	4.2	1.7	1.2
1.5	20	1000	7	4.5	1.9	1.3
1.5	30	130	2	7.8	4.8	3.8
1.5	30	130	3	7.5	4.5	3.4
1.5	30	130	5	6.9	3.7	2.8
1.5	30	130	7	6.9	3.8	2.8
1.5	30	500	2	5.9	2.9	2.1
1.5	30	500	3	5.5	2.6	1.9
1.5	30	500	5	4.8	2.1	1.5
1.5	30	500	7	5.0	2.2	1.6
1.5	30	1000	2	4.3	1.8	1.3
1.5	30	1000	3	3.9	1.6	1.1
1.5	30	1000	5	3.3	1.2	0.8
1.5	30	1000	7	3.5	1.4	1.0
2	10	130	2	8.8	6.3	5.2
2	10	130	3	8.0	5.0	4.0
2	10	130	5	8.2	5.3	4.2
2	10	130	7	8.3	5.5	4.4
2	10	500	2	7.4	4.3	3.3
2	10	500	3	6.6	3.5	2.6
2	10	500	5	6.9	3.7	2.8

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	500	7	7.2	4.0	3.1
2	10	1000	2	5.6	2.6	1.9
2	10	1000	3	5.1	2.3	1.7
2	10	1000	5	5.5	2.6	1.9
2	10	1000	7	5.9	2.9	2.1
2	20	130	2	8.0	5.0	3.9
2	20	130	3	7.3	4.2	3.2
2	20	130	5	7.4	4.3	3.3
2	20	130	7	7.6	4.5	3.4
2	20	500	2	5.8	2.8	2.0
2	20	500	3	5.2	2.3	1.7
2	20	500	5	5.4	2.5	1.8
2	20	500	7	5.8	2.8	2.0
2	20	1000	2	3.7	1.4	1.0
2	20	1000	3	3.6	1.4	1.0
2	20	1000	5	3.9	1.6	1.1
2	20	1000	7	4.3	1.8	1.3
2	30	130	2	7.3	4.1	3.1
2	30	130	3	6.5	3.4	2.5
2	30	130	5	6.7	3.5	2.6
2	30	130	7	6.8	3.7	2.8
2	30	500	2	4.7	2.1	1.5
2	30	500	3	4.2	1.7	1.2
2	30	500	5	4.5	1.9	1.3
2	30	500	7	4.9	2.1	1.5
2	30	1000	2	2.9	1.0	0.7
2	30	1000	3	2.7	1.0	0.7
2	30	1000	5	3.1	1.1	0.8
2	30	1000	7	3.4	1.3	0.9
3.5	10	130	2	7.9	4.9	3.8
3.5	10	130	3	8.0	5.1	4.0
3.5	10	130	5	8.2	5.3	4.2
3.5	10	130	7	8.3	5.5	4.4
3.5	10	500	2	5.9	2.9	2.1
3.5	10	500	3	6.2	3.1	2.3
3.5	10	500	5	6.7	3.6	2.7
3.5	10	500	7	7.0	3.9	2.9
3.5	10	1000	2	4.2	1.8	1.2
3.5	10	1000	3	4.6	2.0	1.4
3.5	10	1000	5	5.2	2.4	1.7
3.5	10	1000	7	5.7	2.7	2.0

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	2	6.8	3.7	2.7
3.5	20	130	3	7.0	3.9	2.9
3.5	20	130	5	7.3	4.2	3.2
3.5	20	130	7	7.4	4.4	3.3
3.5	20	500	2	4.3	1.8	1.3
3.5	20	500	3	4.7	2.0	1.4
3.5	20	500	5	5.2	2.4	1.7
3.5	20	500	7	5.6	2.7	1.9
3.5	20	1000	2	2.8	1.0	0.7
3.5	20	1000	3	3.1	1.2	0.8
3.5	20	1000	5	3.7	1.5	1.0
3.5	20	1000	7	4.1	1.7	1.2
3.5	30	130	2	6.0	2.9	2.1
3.5	30	130	3	6.2	3.1	2.3
3.5	30	130	5	6.5	3.4	2.5
3.5	30	130	7	6.7	3.6	2.7
3.5	30	500	2	3.4	1.3	0.9
3.5	30	500	3	3.7	1.5	1.0
3.5	30	500	5	4.3	1.8	1.2
3.5	30	500	7	4.7	2.0	1.4
3.5	30	1000	2	2.1	0.7	0.5
3.5	30	1000	3	2.4	0.8	0.6
3.5	30	1000	5	2.9	1.1	0.7
3.5	30	1000	7	3.2	1.2	0.8

9.1.3 Estimated Battery Life - Nominal N EOS to EOS Time Estimates

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	9.4	6.7	5.5
1	10	130	3	9.3	6.5	5.3
1	10	130	5	9.1	6.2	5.0
1	10	130	7	8.8	5.8	4.6
1	10	500	2	8.7	5.6	4.4
1	10	500	3	8.4	5.2	4.1
1	10	500	5	7.9	4.6	3.5
1	10	500	7	7.5	4.2	3.2
1	10	1000	2	7.7	4.4	3.4
1	10	1000	3	7.3	4.0	3.1
1	10	1000	5	6.5	3.3	2.5
1	10	1000	7	6.2	3.0	2.2
1	20	130	2	8.6	5.5	4.4
1	20	130	3	8.4	5.3	4.1
1	20	130	5	8.2	4.9	3.8
1	20	130	7	7.7	4.4	3.4
1	20	500	2	7.4	4.1	3.1
1	20	500	3	7.0	3.8	2.8
1	20	500	5	6.3	3.2	2.3
1	20	500	7	5.9	2.9	2.1
1	20	1000	2	6.2	3.0	2.2
1	20	1000	3	5.7	2.7	2.0
1	20	1000	5	4.8	2.1	1.5
1	20	1000	7	4.4	1.9	1.4
1	30	130	2	8.0	4.7	3.6
1	30	130	3	7.7	4.4	3.4
1	30	130	5	7.4	4.1	3.1
1	30	130	7	6.9	3.6	2.7
1	30	500	2	6.5	3.3	2.4
1	30	500	3	6.1	3.0	2.2
1	30	500	5	5.3	2.4	1.8
1	30	500	7	4.9	2.2	1.6
1	30	1000	2	5.1	2.3	1.7
1	30	1000	3	4.7	2.0	1.5
1	30	1000	5	3.9	1.6	1.1
1	30	1000	7	3.3	1.3	0.9
1.5	10	130	2	9.0	6.0	4.9
1.5	10	130	3	8.8	5.7	4.6
1.5	10	130	5	8.4	5.2	4.0

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	7	8.4	5.2	4.1
1.5	10	500	2	7.5	4.2	3.2
1.5	10	500	3	7.2	3.9	3.0
1.5	10	500	5	6.6	3.3	2.5
1.5	10	500	7	6.7	3.5	2.6
1.5	10	1000	2	6.1	3.0	2.2
1.5	10	1000	3	5.7	2.7	2.0
1.5	10	1000	5	5.0	2.2	1.6
1.5	10	1000	7	5.3	2.4	1.7
1.5	20	130	2	7.9	4.7	3.6
1.5	20	130	3	7.6	4.4	3.3
1.5	20	130	5	7.1	3.8	2.8
1.5	20	130	7	7.1	3.8	2.9
1.5	20	500	2	6.0	2.9	2.1
1.5	20	500	3	5.6	2.6	1.9
1.5	20	500	5	4.9	2.2	1.6
1.5	20	500	7	5.1	2.3	1.7
1.5	20	1000	2	4.4	1.9	1.4
1.5	20	1000	3	4.0	1.7	1.2
1.5	20	1000	5	3.1	1.3	0.9
1.5	20	1000	7	3.6	1.5	1.1
1.5	30	130	2	7.1	3.8	2.9
1.5	30	130	3	6.8	3.5	2.6
1.5	30	130	5	6.1	3.0	2.2
1.5	30	130	7	6.2	3.1	2.3
1.5	30	500	2	5.0	2.2	1.6
1.5	30	500	3	4.6	2.0	1.4
1.5	30	500	5	3.9	1.6	1.2
1.5	30	500	7	4.1	1.7	1.2
1.5	30	1000	2	3.2	1.3	0.9
1.5	30	1000	3	2.9	1.1	0.8
1.5	30	1000	5	2.4	0.9	0.7
1.5	30	1000	7	2.6	1.0	0.7
2	10	130	2	8.6	5.5	4.3
2	10	130	3	8.2	5.0	3.9
2	10	130	5	8.2	5.0	3.9
2	10	130	7	8.3	5.1	4.0
2	10	500	2	6.7	3.5	2.6
2	10	500	3	6.0	2.9	2.1
2	10	500	5	6.3	3.1	2.3
2	10	500	7	6.6	3.4	2.5

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	1000	2	5.0	2.2	1.6
2	10	1000	3	4.3	1.8	1.3
2	10	1000	5	4.7	2.0	1.5
2	10	1000	7	5.1	2.3	1.7
2	20	130	2	7.4	4.1	3.1
2	20	130	3	6.8	3.5	2.6
2	20	130	5	6.9	3.6	2.7
2	20	130	7	7.0	3.8	2.8
2	20	500	2	5.0	2.2	1.6
2	20	500	3	4.3	1.8	1.3
2	20	500	5	4.6	2.0	1.4
2	20	500	7	5.0	2.2	1.6
2	20	1000	2	3.0	1.2	0.9
2	20	1000	3	2.6	1.0	0.7
2	20	1000	5	2.9	1.2	0.8
2	20	1000	7	3.3	1.3	0.9
2	30	130	2	6.4	3.2	2.4
2	30	130	3	5.8	2.8	2.0
2	30	130	5	5.9	2.8	2.1
2	30	130	7	6.1	3.0	2.2
2	30	500	2	4.0	1.7	1.2
2	30	500	3	3.2	1.3	0.9
2	30	500	5	3.6	1.5	1.1
2	30	500	7	4.0	1.7	1.2
2	30	1000	2	2.2	0.9	0.6
2	30	1000	3	2.0	0.8	0.6
2	30	1000	5	2.2	0.9	0.6
2	30	1000	7	2.5	1.0	0.7
3.5	10	130	2	7.6	4.3	3.3
3.5	10	130	3	7.8	4.5	3.5
3.5	10	130	5	8.1	4.8	3.7
3.5	10	130	7	8.2	5.0	3.9
3.5	10	500	2	5.1	2.3	1.7
3.5	10	500	3	5.5	2.5	1.8
3.5	10	500	5	6.0	2.9	2.1
3.5	10	500	7	6.4	3.2	2.4
3.5	10	1000	2	3.2	1.3	0.9
3.5	10	1000	3	3.8	1.6	1.1
3.5	10	1000	5	4.4	1.9	1.4
3.5	10	1000	7	4.9	2.2	1.6
3.5	20	130	2	6.1	3.0	2.2

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	3	6.3	3.2	2.3
3.5	20	130	5	6.7	3.4	2.6
3.5	20	130	7	6.9	3.6	2.7
3.5	20	500	2	3.3	1.3	0.9
3.5	20	500	3	3.8	1.6	1.1
3.5	20	500	5	4.3	1.9	1.3
3.5	20	500	7	4.8	2.1	1.5
3.5	20	1000	2	2.0	0.8	0.6
3.5	20	1000	3	2.3	0.9	0.6
3.5	20	1000	5	2.7	1.1	0.8
3.5	20	1000	7	3.1	1.2	0.9
3.5	30	130	2	5.1	2.3	1.7
3.5	30	130	3	5.4	2.5	1.8
3.5	30	130	5	5.7	2.7	2.0
3.5	30	130	7	6.0	2.9	2.1
3.5	30	500	2	2.5	1.0	0.7
3.5	30	500	3	2.8	1.1	0.8
3.5	30	500	5	3.2	1.3	0.9
3.5	30	500	7	3.8	1.6	1.1
3.5	30	1000	2	1.5	0.6	0.4
3.5	30	1000	3	1.7	0.7	0.5
3.5	30	1000	5	2.1	0.8	0.6
3.5	30	1000	7	2.4	0.9	0.7

9.1.4 Estimated Battery Life - Worst Case N EOS to EOS Time Estimates

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	7.7	5.6	4.7
1	10	130	3	7.8	5.7	4.8
1	10	130	5	7.2	4.9	4.0
1	10	130	7	7.2	4.9	3.9
1	10	500	2	7.6	5.4	4.4
1	10	500	3	7.3	5.0	4.1
1	10	500	5	6.7	4.2	3.3
1	10	500	7	6.5	3.9	3.0
1	10	1000	2	6.8	4.2	3.3
1	10	1000	3	6.6	4.0	3.1
1	10	1000	5	5.9	3.2	2.4
1	10	1000	7	5.5	2.9	2.2
1	20	130	2	7.5	5.3	4.4
1	20	130	3	7.4	5.1	4.1
1	20	130	5	7.1	4.7	3.7
1	20	130	7	6.7	4.1	3.2
1	20	500	2	6.7	4.1	3.2
1	20	500	3	6.4	3.8	2.9
1	20	500	5	5.6	3.0	2.2
1	20	500	7	5.4	2.8	2.1
1	20	1000	2	5.6	2.9	2.2
1	20	1000	3	5.3	2.8	2.1
1	20	1000	5	4.6	2.2	1.6
1	20	1000	7	4.1	1.9	1.4
1	30	130	2	7.1	4.6	3.7
1	30	130	3	6.9	4.4	3.5
1	30	130	5	6.5	3.9	3.0
1	30	130	7	6.1	3.5	2.7
1	30	500	2	6.0	3.4	2.6
1	30	500	3	5.7	3.0	2.3
1	30	500	5	4.9	2.4	1.8
1	30	500	7	4.6	2.2	1.6
1	30	1000	2	4.6	2.2	1.6
1	30	1000	3	4.5	2.1	1.6
1	30	1000	5	3.8	1.7	1.2
1	30	1000	7	3.1	1.3	0.9
1.5	10	130	2	7.6	5.5	4.6
1.5	10	130	3	7.4	5.1	4.2
1.5	10	130	5	6.8	4.3	3.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	7	6.8	4.3	3.4
1.5	10	500	2	6.4	3.8	3.0
1.5	10	500	3	6.4	3.8	2.9
1.5	10	500	5	5.7	3.1	2.3
1.5	10	500	7	5.9	3.3	2.5
1.5	10	1000	2	5.6	3.0	2.3
1.5	10	1000	3	5.3	2.7	2.0
1.5	10	1000	5	4.6	2.2	1.6
1.5	10	1000	7	4.8	2.4	1.7
1.5	20	130	2	7.0	4.5	3.6
1.5	20	130	3	6.7	4.2	3.3
1.5	20	130	5	6.2	3.5	2.7
1.5	20	130	7	6.2	3.6	2.7
1.5	20	500	2	5.6	3.0	2.2
1.5	20	500	3	5.2	2.7	2.0
1.5	20	500	5	4.6	2.2	1.6
1.5	20	500	7	4.7	2.3	1.7
1.5	20	1000	2	4.3	2.0	1.4
1.5	20	1000	3	3.9	1.7	1.3
1.5	20	1000	5	3.1	1.3	0.9
1.5	20	1000	7	3.5	1.5	1.1
1.5	30	130	2	6.4	3.8	2.9
1.5	30	130	3	6.1	3.5	2.7
1.5	30	130	5	5.5	2.9	2.2
1.5	30	130	7	5.6	3.0	2.2
1.5	30	500	2	4.8	2.3	1.7
1.5	30	500	3	4.4	2.1	1.5
1.5	30	500	5	3.8	1.7	1.2
1.5	30	500	7	4.0	1.8	1.3
1.5	30	1000	2	3.3	1.4	1.0
1.5	30	1000	3	2.9	1.2	0.9
1.5	30	1000	5	2.4	1.0	0.7
1.5	30	1000	7	2.6	1.1	0.8
2	10	130	2	7.3	4.9	4.0
2	10	130	3	6.5	4.0	3.1
2	10	130	5	6.7	4.2	3.3
2	10	130	7	6.8	4.3	3.4
2	10	500	2	6.0	3.4	2.6
2	10	500	3	5.4	2.8	2.1
2	10	500	5	5.5	2.9	2.2
2	10	500	7	5.8	3.2	2.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	1000	2	4.5	2.1	1.5
2	10	1000	3	4.1	1.9	1.3
2	10	1000	5	4.4	2.1	1.5
2	10	1000	7	4.7	2.3	1.7
2	20	130	2	6.5	3.9	3.1
2	20	130	3	5.9	3.3	2.5
2	20	130	5	6.0	3.4	2.6
2	20	130	7	6.1	3.5	2.7
2	20	500	2	4.7	2.2	1.6
2	20	500	3	4.1	1.9	1.4
2	20	500	5	4.3	2.0	1.5
2	20	500	7	4.6	2.2	1.6
2	20	1000	2	2.7	1.1	0.8
2	20	1000	3	2.7	1.1	0.8
2	20	1000	5	2.9	1.2	0.9
2	20	1000	7	3.2	1.4	1.0
2	30	130	2	5.9	3.3	2.5
2	30	130	3	5.3	2.7	2.0
2	30	130	5	5.4	2.8	2.1
2	30	130	7	5.5	2.9	2.2
2	30	500	2	3.8	1.7	1.2
2	30	500	3	3.1	1.3	0.9
2	30	500	5	3.6	1.5	1.1
2	30	500	7	3.9	1.7	1.2
2	30	1000	2	2.1	0.8	0.6
2	30	1000	3	2.0	0.8	0.6
2	30	1000	5	2.3	0.9	0.7
2	30	1000	7	2.6	1.0	0.7
3.5	10	130	2	6.4	3.8	3.0
3.5	10	130	3	6.6	4.0	3.1
3.5	10	130	5	6.7	4.2	3.3
3.5	10	130	7	6.8	4.3	3.4
3.5	10	500	2	4.7	2.3	1.7
3.5	10	500	3	5.0	2.5	1.8
3.5	10	500	5	5.4	2.8	2.1
3.5	10	500	7	5.7	3.1	2.3
3.5	10	1000	2	3.2	1.3	1.0
3.5	10	1000	3	3.7	1.6	1.2
3.5	10	1000	5	4.2	1.9	1.4
3.5	10	1000	7	4.6	2.2	1.6
3.5	20	130	2	5.5	2.9	2.2

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	3	5.7	3.0	2.3
3.5	20	130	5	5.9	3.3	2.5
3.5	20	130	7	6.1	3.4	2.6
3.5	20	500	2	3.2	1.4	1.0
3.5	20	500	3	3.7	1.6	1.2
3.5	20	500	5	4.2	1.9	1.4
3.5	20	500	7	4.5	2.1	1.5
3.5	20	1000	2	2.1	0.8	0.6
3.5	20	1000	3	2.3	0.9	0.7
3.5	20	1000	5	2.8	1.1	0.8
3.5	20	1000	7	3.1	1.3	0.9
3.5	30	130	2	4.8	2.3	1.7
3.5	30	130	3	5.0	2.5	1.8
3.5	30	130	5	5.2	2.7	2.0
3.5	30	130	7	5.4	2.8	2.1
3.5	30	500	2	2.5	1.0	0.7
3.5	30	500	3	2.8	1.1	0.8
3.5	30	500	5	3.2	1.3	1.0
3.5	30	500	7	3.7	1.6	1.2
3.5	30	1000	2	1.6	0.6	0.5
3.5	30	1000	3	1.8	0.7	0.5
3.5	30	1000	5	2.1	0.8	0.6
3.5	30	1000	7	2.4	1.0	0.7

9.2 Appendix B — Model 103/104 Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms (M103/104)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	2.8	2.5	2.4	2.2	2.0	1.9
0.5	15	130	>10	>10	>10	2.7	2.2	1.9	2.1	1.7	1.5
0.5	20	130	>10	>10	>10	2.5	1.9	1.7	2.0	1.5	1.3
0.5	25	130	>10	>10	>10	2.4	1.7	1.4	1.9	1.4	1.2
0.5	30	130	>10	>10	9.5	2.3	1.6	1.3	1.8	1.3	1.0
0.5	10	250	>10	>10	>10	2.7	2.3	2.0	2.1	1.8	1.6
0.5	15	250	>10	>10	>10	2.5	1.9	1.6	2.0	1.5	1.3
0.5	20	250	>10	>10	>10	2.4	1.7	1.4	1.9	1.3	1.1
0.5	25	250	>10	>10	8.7	2.3	1.5	1.2	1.8	1.2	0.9
0.5	30	250	>10	9.8	7.6	2.1	1.3	1.0	1.7	1.0	0.8
0.5	10	500	>10	>10	>10	2.5	1.9	1.6	1.9	1.5	1.2
0.5	15	500	>10	>10	8.9	2.3	1.5	1.2	1.8	1.2	0.9
0.5	20	500	>10	9.3	7.2	2.1	1.2	1.0	1.6	1.0	0.8
0.5	25	500	>10	8.1	6.1	1.9	1.1	0.8	1.5	0.9	0.6
0.5	30	500	>10	7.1	5.2	1.8	0.9	0.7	1.4	0.8	0.6
0.5	10	750	>10	>10	9.4	2.3	1.6	1.3	1.8	1.2	1.0
0.5	15	750	>10	9.1	7.0	2.1	1.2	0.9	1.6	1.0	0.7
0.5	20	750	>10	7.5	5.6	1.9	1.0	0.7	1.5	0.8	0.6
0.5	25	750	>10	6.4	4.7	1.7	0.9	0.6	1.3	0.7	0.5
0.5	30	750	>10	5.5	4.0	1.5	0.7	0.5	1.2	0.6	0.4
0.5	10	1000	>10	>10	7.9	2.2	1.4	1.1	1.7	1.1	0.8
0.5	15	1000	>10	7.7	5.8	1.9	1.0	0.8	1.5	0.8	0.6
0.5	20	1000	>10	6.3	4.6	1.7	0.8	0.6	1.3	0.7	0.5
0.5	25	1000	>10	5.3	3.8	1.5	0.7	0.5	1.2	0.6	0.4
0.5	30	1000	>10	4.6	3.2	1.4	0.6	0.4	1.1	0.5	0.3
1	10	130	>10	>10	>10	2.6	2.1	1.9	2.0	1.5	1.3
1	15	130	>10	>10	>10	2.5	1.9	1.6	1.9	1.4	1.1
1	20	130	>10	>10	>10	2.4	1.6	1.3	1.8	1.2	0.9
1	25	130	>10	>10	9.3	2.2	1.5	1.2	1.7	1.1	0.8
1	30	130	>10	>10	8.2	2.1	1.3	1.0	1.6	1.0	0.8
1	10	250	>10	>10	>10	2.4	1.7	1.4	1.8	1.3	1.0
1	15	250	>10	>10	8.9	2.2	1.4	1.1	1.7	1.1	0.9
1	20	250	>10	9.4	7.2	2.1	1.2	0.9	1.6	0.9	0.7
1	25	250	>10	8.1	6.1	1.9	1.1	0.8	1.5	0.8	0.6
1	30	250	>10	7.1	5.3	1.8	0.9	0.7	1.4	0.7	0.5
1	10	500	>10	>10	7.9	2.1	1.2	1.0	1.5	0.9	0.7

Parameters at 3kOhms (M103/104)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	15	500	>10	7.8	5.8	1.8	1.0	0.7	1.4	0.7	0.5
1	20	500	>10	6.3	4.6	1.6	0.8	0.6	1.2	0.6	0.4
1	25	500	>10	5.3	3.8	1.5	0.7	0.5	1.1	0.5	0.4
1	30	500	>10	4.6	3.2	1.3	0.6	0.4	1.0	0.4	0.3
1	10	750	>10	8.0	6.0	1.8	1.0	0.7	1.3	0.7	0.5
1	15	750	>10	6.0	4.3	1.5	0.7	0.5	1.1	0.5	0.4
1	20	750	>10	4.7	3.4	1.3	0.6	0.4	1.0	0.4	0.3
1	25	750	9.3	3.9	2.8	1.2	0.5	0.3	0.9	0.4	0.3
1	30	750	8.3	3.4	2.3	1.1	0.4	0.3	0.8	0.3	0.2
1	10	1000	>10	6.6	4.9	1.6	0.8	0.6	1.2	0.5	0.4
1	15	1000	>10	4.8	3.4	1.3	0.6	0.4	1.0	0.4	0.3
1	20	1000	9.0	3.8	2.7	1.1	0.5	0.3	0.8	0.3	0.2
1	25	1000	7.8	3.1	2.2	1.0	0.4	0.3	0.7	0.3	0.2
1	30	1000	6.9	2.7	1.8	0.9	0.3	0.2	0.6	0.2	0.2
1.5	10	130	>10	>10	8.8	2.2	1.4	1.1	1.6	1.0	0.8
1.5	15	130	>10	>10	7.9	2.1	1.3	1.0	1.6	0.9	0.7
1.5	20	130	>10	9.3	7.1	2.0	1.1	0.9	1.5	0.8	0.6
1.5	25	130	>10	8.3	6.3	1.9	1.0	0.8	1.4	0.7	0.5
1.5	30	130	>10	7.6	5.7	1.8	0.9	0.7	1.3	0.6	0.5
1.5	10	250	>10	>10	8.8	2.1	1.3	1.0	1.5	0.8	0.6
1.5	15	250	>10	8.9	6.8	1.9	1.0	0.8	1.3	0.7	0.5
1.5	20	250	>10	7.5	5.6	1.7	0.9	0.6	1.2	0.6	0.4
1.5	25	250	>10	6.4	4.7	1.6	0.8	0.5	1.1	0.5	0.4
1.5	30	250	>10	5.6	4.0	1.4	0.7	0.5	1.0	0.5	0.3
1.5	10	500	>10	7.3	5.4	1.7	0.8	0.6	1.2	0.6	0.4
1.5	15	500	>10	5.7	4.1	1.4	0.7	0.5	1.0	0.4	0.3
1.5	20	500	>10	4.7	3.3	1.2	0.5	0.4	0.9	0.4	0.2
1.5	25	500	9.2	3.9	2.7	1.1	0.4	0.3	0.8	0.3	0.2
1.5	30	500	8.2	3.3	2.3	1.0	0.4	0.3	0.7	0.3	0.2
1.5	10	750	>10	5.3	3.8	1.4	0.6	0.4	0.9	0.4	0.3
1.5	15	750	9.5	4.1	2.9	1.1	0.5	0.3	0.8	0.3	0.2
1.5	20	750	8.1	3.3	2.3	1.0	0.4	0.3	0.6	0.2	0.2
1.5	25	750	7.0	2.7	1.9	0.8	0.3	0.2	0.6	0.2	0.1
1.5	30	750	6.2	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
1.5	10	1000	9.7	4.2	3.0	1.1	0.5	0.3	0.8	0.3	0.2
1.5	15	1000	7.8	3.1	2.2	0.9	0.4	0.2	0.6	0.2	0.2
1.5	20	1000	6.5	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
1.5	25	1000	5.6	2.1	1.4	0.7	0.2	0.2	0.4	0.2	0.1
1.5	30	1000	4.9	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1

Parameters at 3kOhms (M103/104)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2	10	130	>10	8.7	6.6	1.9	1.1	0.8	1.4	0.7	0.5
2	15	130	>10	7.2	5.3	1.7	0.9	0.6	1.2	0.6	0.4
2	20	130	>10	6.2	4.5	1.6	0.8	0.5	1.1	0.5	0.4
2	25	130	>10	5.5	4.0	1.4	0.7	0.5	1.0	0.5	0.3
2	30	130	>10	5.0	3.5	1.3	0.6	0.4	1.0	0.4	0.3
2	10	250	>10	6.4	4.7	1.6	0.8	0.6	1.2	0.5	0.4
2	15	250	>10	5.2	3.8	1.4	0.6	0.4	1.0	0.4	0.3
2	20	250	>10	4.4	3.1	1.2	0.5	0.4	0.9	0.4	0.3
2	25	250	9.1	3.8	2.7	1.1	0.5	0.3	0.8	0.3	0.2
2	30	250	8.3	3.4	2.3	1.0	0.4	0.3	0.7	0.3	0.2
2	10	500	9.5	4.1	2.9	1.2	0.5	0.3	0.8	0.3	0.2
2	15	500	7.8	3.1	2.2	1.0	0.4	0.3	0.7	0.3	0.2
2	20	500	6.7	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
2	25	500	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
2	30	500	5.2	1.9	1.3	0.6	0.2	0.1	0.4	0.1	0.1
2	10	750	7.5	2.9	2.0	0.9	0.3	0.2	0.6	0.2	0.2
2	15	750	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
2	20	750	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
2	25	750	4.3	1.5	1.0	0.5	0.2	0.1	0.3	0.1	0.1
2	30	750	3.7	1.3	0.9	0.4	0.1	0.1	0.3	0.1	0.1
2	10	1000	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
2	15	1000	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
2	20	1000	3.9	1.3	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2	25	1000	3.3	1.1	0.8	0.4	0.1	0.1	0.3	0.1	0.1
2	30	1000	2.9	1.0	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	7.2	5.3	1.7	0.9	0.6	1.3	0.6	0.5
2.5	15	130	>10	6.0	4.4	1.5	0.7	0.5	1.1	0.5	0.4
2.5	20	130	>10	5.1	3.7	1.4	0.6	0.4	1.0	0.4	0.3
2.5	25	130	>10	4.5	3.2	1.2	0.5	0.4	0.9	0.4	0.3
2.5	30	130	9.3	4.0	2.8	1.1	0.5	0.3	0.8	0.3	0.2
2.5	10	250	>10	5.4	3.9	1.4	0.6	0.5	1.0	0.4	0.3
2.5	15	250	9.6	4.1	2.9	1.2	0.5	0.3	0.8	0.3	0.2
2.5	20	250	8.4	3.4	2.4	1.0	0.4	0.3	0.7	0.3	0.2
2.5	25	250	7.4	2.9	2.0	0.9	0.3	0.2	0.6	0.2	0.2
2.5	30	250	6.7	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
2.5	10	500	8.0	3.2	2.2	1.0	0.4	0.3	0.7	0.3	0.2
2.5	15	500	6.3	2.4	1.6	0.8	0.3	0.2	0.5	0.2	0.1
2.5	20	500	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.2	0.1
2.5	25	500	4.6	1.6	1.1	0.5	0.2	0.1	0.4	0.1	0.1

Parameters at 3kOhms (M103/104)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	30	500	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2.5	10	750	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
2.5	15	750	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	20	750	3.9	1.3	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2.5	25	750	3.3	1.1	0.7	0.4	0.1	0.1	0.3	0.1	0.1
2.5	30	750	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	1000	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	3.7	1.3	0.9	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	3.0	1.0	0.7	0.4	0.1	0.1	0.2	0.1	0.1
2.5	25	1000	2.5	0.8	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	2.2	0.7	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	6.3	4.6	1.6	0.7	0.5	1.1	0.5	0.4
3	15	130	>10	5.0	3.6	1.3	0.6	0.4	1.0	0.4	0.3
3	20	130	9.6	4.2	2.9	1.2	0.5	0.3	0.8	0.3	0.2
3	25	130	8.6	3.6	2.5	1.0	0.4	0.3	0.7	0.3	0.2
3	30	130	7.8	3.1	2.2	0.9	0.4	0.3	0.7	0.2	0.2
3	10	250	>10	4.4	3.1	1.2	0.5	0.4	0.8	0.3	0.2
3	15	250	8.1	3.3	2.3	1.0	0.4	0.3	0.7	0.3	0.2
3	20	250	6.8	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
3	25	250	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
3	30	250	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.1	0.1
3	10	500	6.6	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
3	15	500	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
3	20	500	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
3	25	500	3.4	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3	30	500	3.0	1.0	0.7	0.3	0.1	0.1	0.2	0.1	0.1
3	10	750	4.9	1.7	1.2	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	3.6	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3	20	750	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
3	25	750	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	30	750	2.0	0.7	0.4	0.2	0.1	0.1	0.2	0.1	0.0
3	10	1000	3.8	1.3	0.9	0.4	0.2	0.1	0.3	0.1	0.1
3	15	1000	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	2.2	0.7	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	1.8	0.6	0.4	0.2	0.1	0.0	0.1	0.0	0.0
3	30	1000	1.5	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	4.7	3.4	1.3	0.6	0.4	0.9	0.4	0.3
3.5	15	130	9.0	3.8	2.6	1.1	0.4	0.3	0.8	0.3	0.2
3.5	20	130	7.7	3.1	2.1	0.9	0.4	0.3	0.6	0.2	0.2

Parameters at 3kOhms (M103/104)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3.5	25	130	6.8	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
3.5	30	130	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
3.5	10	250	8.0	3.2	2.2	1.0	0.4	0.3	0.7	0.3	0.2
3.5	15	250	6.4	2.4	1.7	0.8	0.3	0.2	0.5	0.2	0.1
3.5	20	250	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.2	0.1
3.5	25	250	4.6	1.6	1.1	0.5	0.2	0.1	0.4	0.1	0.1
3.5	30	250	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
3.5	10	500	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	15	500	3.6	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3.5	20	500	3.0	1.0	0.7	0.3	0.1	0.1	0.2	0.1	0.1
3.5	25	500	2.5	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	30	500	2.1	0.7	0.5	0.2	0.1	0.1	0.2	0.1	0.0
3.5	10	750	3.2	1.1	0.7	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	2.0	0.6	0.4	0.2	0.1	0.0	0.2	0.1	0.0
3.5	25	750	1.7	0.5	0.4	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	750	1.4	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	1000	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	1.9	0.6	0.4	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	1.5	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	1.3	0.4	0.3	0.1	0.0	0.0	0.1	0.0	0.0
3.5	30	1000	1.1	0.3	0.2	0.1	0.0	0.0	0.1	0.0	0.0

9.3 Appendix C — Model 105 Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	0.9
0.5	15	130	>10	>10	>10	2.5	1.5	1.2	1.8	1.1	0.9
0.5	20	130	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	25	130	>10	>10	>10	2.2	1.3	1.0	1.7	1.0	0.7
0.5	30	130	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	10	250	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	1.0
0.5	15	250	>10	>10	>10	2.4	1.4	1.1	1.8	1.1	0.8
0.5	20	250	>10	>10	>10	2.3	1.3	1.0	1.7	1.0	0.7
0.5	25	250	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	30	250	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
0.5	10	500	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	15	500	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	20	500	>10	>10	>10	2.0	1.1	0.8	1.5	0.8	0.6
0.5	25	500	>10	>10	9.0	1.9	0.9	0.7	1.4	0.7	0.5
0.5	30	500	>10	>10	8.6	1.8	0.9	0.6	1.3	0.7	0.5
0.5	10	750	>10	>10	>10	2.2	1.3	1.0	1.7	0.9	0.7
0.5	15	750	>10	>10	>10	2.0	1.1	0.8	1.5	0.8	0.6
0.5	20	750	>10	>10	8.9	1.9	0.9	0.7	1.4	0.7	0.5
0.5	25	750	>10	>10	7.7	1.7	0.8	0.6	1.3	0.6	0.4
0.5	30	750	>10	9.6	6.8	1.6	0.7	0.5	1.2	0.5	0.4
0.5	10	1000	>10	>10	>10	2.1	1.2	0.9	1.6	0.9	0.6
0.5	15	1000	>10	>10	8.9	1.9	0.9	0.7	1.4	0.7	0.5
0.5	20	1000	>10	>10	7.3	1.7	0.8	0.6	1.2	0.6	0.4
0.5	25	1000	>10	9.2	6.5	1.5	0.7	0.5	1.1	0.5	0.4
0.5	30	1000	>10	8.0	5.7	1.4	0.6	0.4	1.0	0.4	0.3
1	10	130	>10	>10	>10	2.4	1.4	1.1	1.7	0.9	0.7
1	15	130	>10	>10	>10	2.3	1.4	1.0	1.6	0.9	0.7
1	20	130	>10	>10	>10	2.3	1.3	1.0	1.6	0.9	0.7
1	25	130	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	30	130	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
1	10	250	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	15	250	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
1	20	250	>10	>10	>10	2.0	1.0	0.7	1.4	0.7	0.5
1	25	250	>10	>10	9.7	1.9	0.9	0.7	1.3	0.6	0.5
1	30	250	>10	>10	8.9	1.8	0.8	0.6	1.2	0.6	0.4

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	10	500	>10	>10	>10	2.0	1.0	0.7	1.3	0.6	0.5
1	15	500	>10	>10	9.6	1.8	0.8	0.6	1.2	0.5	0.4
1	20	500	>10	>10	7.8	1.6	0.7	0.5	1.1	0.5	0.3
1	25	500	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
1	30	500	>10	8.4	5.9	1.3	0.6	0.4	0.9	0.4	0.3
1	10	750	>10	>10	9.7	1.7	0.8	0.6	1.2	0.5	0.4
1	15	750	>10	>10	7.4	1.5	0.7	0.5	1.0	0.4	0.3
1	20	750	>10	8.6	6.0	1.3	0.6	0.4	0.9	0.4	0.3
1	25	750	>10	7.3	5.1	1.2	0.5	0.3	0.8	0.3	0.2
1	30	750	>10	6.4	4.4	1.1	0.4	0.3	0.7	0.3	0.2
1	10	1000	>10	>10	8.0	1.5	0.7	0.5	1.0	0.4	0.3
1	15	1000	>10	8.8	6.2	1.3	0.5	0.4	0.9	0.4	0.2
1	20	1000	>10	7.1	4.9	1.1	0.5	0.3	0.8	0.3	0.2
1	25	1000	>10	6.0	4.1	1.0	0.4	0.3	0.7	0.3	0.2
1	30	1000	>10	5.1	3.5	0.9	0.3	0.2	0.6	0.2	0.2
1.5	10	130	>10	>10	>10	2.0	1.1	0.8	1.5	0.7	0.6
1.5	15	130	>10	>10	>10	1.9	1.0	0.7	1.4	0.7	0.5
1.5	20	130	>10	>10	9.4	1.8	0.9	0.7	1.3	0.6	0.5
1.5	25	130	>10	>10	8.8	1.8	0.8	0.6	1.3	0.6	0.4
1.5	30	130	>10	>10	7.8	1.7	0.8	0.6	1.2	0.6	0.4
1.5	10	250	>10	>10	9.3	1.8	0.9	0.6	1.3	0.6	0.4
1.5	15	250	>10	>10	7.9	1.6	0.7	0.5	1.1	0.5	0.4
1.5	20	250	>10	>10	7.6	1.6	0.7	0.5	1.1	0.5	0.3
1.5	25	250	>10	9.1	6.5	1.4	0.6	0.4	1.0	0.4	0.3
1.5	30	250	>10	8.5	6.0	1.3	0.6	0.4	0.9	0.4	0.3
1.5	10	500	>10	9.4	6.6	1.4	0.6	0.4	1.0	0.4	0.3
1.5	15	500	>10	7.4	5.2	1.2	0.5	0.3	0.8	0.3	0.2
1.5	20	500	>10	6.5	4.5	1.1	0.4	0.3	0.7	0.3	0.2
1.5	25	500	>10	5.7	4.0	1.0	0.4	0.3	0.7	0.2	0.2
1.5	30	500	>10	5.1	3.5	0.9	0.3	0.2	0.6	0.2	0.1
1.5	10	750	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
1.5	15	750	>10	5.5	3.8	1.0	0.4	0.2	0.7	0.2	0.2
1.5	20	750	>10	4.7	3.2	0.8	0.3	0.2	0.6	0.2	0.1
1.5	25	750	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
1.5	30	750	10.0	3.6	2.4	0.7	0.2	0.2	0.4	0.2	0.1
1.5	10	1000	>10	5.7	4.0	1.0	0.4	0.3	0.7	0.2	0.2
1.5	15	1000	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
1.5	20	1000	9.9	3.5	2.4	0.7	0.2	0.2	0.4	0.2	0.1

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1.5	25	1000	8.7	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
1.5	30	1000	7.8	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
2	10	130	>10	>10	9.4	1.8	0.9	0.6	1.3	0.6	0.4
2	15	130	>10	>10	8.0	1.7	0.8	0.5	1.2	0.5	0.4
2	20	130	>10	9.8	7.0	1.5	0.7	0.5	1.1	0.5	0.3
2	25	130	>10	8.8	6.2	1.4	0.6	0.4	1.0	0.4	0.3
2	30	130	>10	8.1	5.7	1.3	0.6	0.4	0.9	0.4	0.3
2	10	250	>10	9.7	6.9	1.5	0.7	0.5	1.0	0.4	0.3
2	15	250	>10	8.2	5.7	1.3	0.5	0.4	0.9	0.4	0.3
2	20	250	>10	6.8	4.7	1.1	0.5	0.3	0.8	0.3	0.2
2	25	250	>10	5.9	4.1	1.0	0.4	0.3	0.7	0.3	0.2
2	30	250	>10	5.2	3.6	0.9	0.4	0.2	0.6	0.2	0.2
2	10	500	>10	6.5	4.5	1.1	0.4	0.3	0.7	0.3	0.2
2	15	500	>10	5.0	3.4	0.9	0.3	0.2	0.6	0.2	0.1
2	20	500	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2	25	500	9.6	3.4	2.3	0.7	0.2	0.2	0.4	0.2	0.1
2	30	500	8.7	3.0	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2	10	750	>10	4.8	3.3	0.9	0.3	0.2	0.6	0.2	0.1
2	15	750	>10	3.6	2.4	0.7	0.2	0.2	0.4	0.2	0.1
2	20	750	8.1	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	25	750	7.0	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
2	30	750	6.2	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
2	10	1000	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
2	15	1000	8.0	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	20	1000	6.5	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2	25	1000	5.5	1.8	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2	30	1000	4.8	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	>10	8.3	1.7	0.8	0.6	1.2	0.5	0.4
2.5	15	130	>10	9.6	6.8	1.5	0.6	0.5	1.0	0.4	0.3
2.5	20	130	>10	8.5	6.0	1.4	0.6	0.4	0.9	0.4	0.3
2.5	25	130	>10	7.4	5.2	1.2	0.5	0.4	0.9	0.3	0.2
2.5	30	130	>10	6.7	4.7	1.1	0.5	0.3	0.8	0.3	0.2
2.5	10	250	>10	8.3	5.9	1.3	0.6	0.4	0.9	0.4	0.3
2.5	15	250	>10	6.5	4.5	1.1	0.4	0.3	0.8	0.3	0.2
2.5	20	250	>10	5.5	3.8	1.0	0.4	0.3	0.7	0.2	0.2
2.5	25	250	>10	4.6	3.2	0.8	0.3	0.2	0.6	0.2	0.1
2.5	30	250	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
2.5	10	500	>10	5.4	3.7	0.9	0.4	0.2	0.6	0.2	0.2

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	15	500	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2.5	20	500	9.0	3.2	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	25	500	7.8	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
2.5	30	500	6.8	2.3	1.5	0.5	0.2	0.1	0.3	0.1	0.1
2.5	10	750	>10	3.9	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2.5	15	750	8.2	2.9	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2.5	20	750	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	25	750	5.5	1.8	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2.5	30	750	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	1000	8.8	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	6.5	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	5.2	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	25	1000	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	>10	7.3	1.5	0.7	0.5	1.1	0.5	0.3
3	15	130	>10	8.5	6.0	1.3	0.6	0.4	0.9	0.4	0.3
3	20	130	>10	7.4	5.1	1.2	0.5	0.3	0.8	0.3	0.2
3	25	130	>10	6.2	4.3	1.1	0.4	0.3	0.7	0.3	0.2
3	30	130	>10	5.5	3.8	1.0	0.4	0.3	0.7	0.2	0.2
3	10	250	>10	6.9	4.8	1.2	0.5	0.3	0.8	0.3	0.2
3	15	250	>10	5.3	3.7	0.9	0.4	0.2	0.6	0.2	0.2
3	20	250	>10	4.4	3.0	0.8	0.3	0.2	0.5	0.2	0.1
3	25	250	>10	3.7	2.5	0.7	0.2	0.2	0.5	0.2	0.1
3	30	250	9.2	3.2	2.2	0.6	0.2	0.1	0.4	0.1	0.1
3	10	500	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3	15	500	8.7	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3	20	500	7.1	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
3	25	500	6.1	2.0	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	30	500	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0
3	10	750	8.4	2.9	2.0	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	6.3	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	20	750	5.1	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	25	750	4.2	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3	30	750	3.6	1.2	0.8	0.2	0.1	0.1	0.2	0.0	0.0
3	10	1000	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	1000	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	3.9	1.3	0.8	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	3.2	1.0	0.7	0.2	0.1	0.0	0.1	0.0	0.0

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3	30	1000	2.7	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	6.7	4.7	1.2	0.5	0.3	0.9	0.4	0.2
3.5	15	130	>10	6.0	4.1	1.1	0.4	0.3	0.8	0.3	0.2
3.5	20	130	>10	5.0	3.4	0.9	0.4	0.2	0.7	0.2	0.2
3.5	25	130	>10	4.6	3.1	0.8	0.3	0.2	0.6	0.2	0.1
3.5	30	130	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3.5	10	250	>10	4.6	3.1	0.9	0.3	0.2	0.6	0.2	0.1
3.5	15	250	>10	3.6	2.5	0.7	0.2	0.2	0.5	0.2	0.1
3.5	20	250	8.7	3.0	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	25	250	7.5	2.6	1.7	0.5	0.2	0.1	0.3	0.1	0.1
3.5	30	250	6.7	2.3	1.5	0.5	0.2	0.1	0.3	0.1	0.1
3.5	10	500	7.2	2.4	1.6	0.5	0.2	0.1	0.4	0.1	0.1
3.5	15	500	5.9	2.0	1.3	0.4	0.1	0.1	0.3	0.1	0.1
3.5	20	500	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3.5	25	500	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	30	500	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3.5	10	750	5.2	1.7	1.1	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	4.1	1.3	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	25	750	3.0	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	750	2.6	0.8	0.5	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	1000	4.4	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	2.3	0.7	0.5	0.2	0.0	0.0	0.1	0.0	0.0
3.5	30	1000	2.0	0.6	0.4	0.1	0.0	0.0	0.1	0.0	0.0

9.4 Appendix D — Model 106 Battery Longevity and Programmed Setting Choices

9.4.1 AutoStim Feature Disabled

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	3.0	2.5	2.2	2.2	1.8	1.6
0.5	10	250	>10	>10	>10	2.9	2.3	2.0	2.2	1.7	1.5
0.5	10	500	>10	>10	>10	2.7	1.9	1.6	2.0	1.4	1.2
0.5	10	750	>10	>10	>10	2.6	1.7	1.3	1.9	1.2	1.0
0.5	10	1000	>10	>10	>10	2.4	1.5	1.1	1.8	1.1	0.8
0.5	15	130	>10	>10	>10	2.9	2.2	1.9	2.1	1.6	1.4
0.5	15	250	>10	>10	>10	2.8	2.0	1.7	2.1	1.5	1.2
0.5	15	500	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	0.9
0.5	15	750	>10	>10	>10	2.3	1.4	1.0	1.7	1.0	0.8
0.5	15	1000	>10	>10	>10	2.1	1.2	0.9	1.6	0.9	0.6
0.5	20	130	>10	>10	>10	2.8	2.0	1.7	2.1	1.5	1.2
0.5	20	250	>10	>10	>10	2.7	1.8	1.5	2.0	1.3	1.1
0.5	20	500	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	20	750	>10	>10	>10	2.1	1.1	0.9	1.6	0.8	0.6
0.5	20	1000	>10	>10	9.3	1.9	1.0	0.7	1.4	0.7	0.5
0.5	25	130	>10	>10	>10	2.7	1.8	1.5	2.0	1.4	1.1
0.5	25	250	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	1.0
0.5	25	500	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	25	750	>10	>10	9.6	1.9	1.0	0.7	1.4	0.7	0.5
0.5	25	1000	>10	>10	7.8	1.7	0.8	0.6	1.3	0.6	0.4
0.5	30	130	>10	>10	>10	2.6	1.7	1.3	1.9	1.3	1.0
0.5	30	250	>10	>10	>10	2.4	1.5	1.2	1.8	1.1	0.9
0.5	30	500	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
0.5	30	750	>10	>10	8.3	1.8	0.9	0.6	1.3	0.6	0.5
0.5	30	1000	>10	9.5	6.7	1.6	0.7	0.5	1.2	0.5	0.4
1	10	130	>10	>10	>10	2.7	1.8	1.5	1.9	1.2	1.0
1	10	250	>10	>10	>10	2.5	1.6	1.2	1.7	1.0	0.8
1	10	500	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	10	750	>10	>10	>10	2.0	1.0	0.7	1.3	0.6	0.4
1	10	1000	>10	>10	9.7	1.8	0.8	0.6	1.1	0.5	0.4
1	15	130	>10	>10	>10	2.6	1.7	1.4	1.8	1.2	0.9
1	15	250	>10	>10	>10	2.4	1.4	1.1	1.6	0.9	0.7
1	15	500	>10	>10	>10	2.0	1.1	0.8	1.3	0.7	0.5
1	15	750	>10	>10	8.7	1.7	0.8	0.6	1.1	0.5	0.4

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	15	1000	>10	9.8	7.0	1.5	0.7	0.5	1.0	0.4	0.3
1	20	130	>10	>10	>10	2.5	1.6	1.3	1.8	1.1	0.9
1	20	250	>10	>10	>10	2.3	1.3	1.0	1.6	0.8	0.6
1	20	500	>10	>10	9.3	1.8	0.9	0.7	1.2	0.6	0.4
1	20	750	>10	9.7	6.9	1.5	0.7	0.5	1.0	0.4	0.3
1	20	1000	>10	7.8	5.5	1.3	0.5	0.4	0.8	0.3	0.2
1	25	130	>10	>10	>10	2.4	1.5	1.2	1.7	1.0	0.8
1	25	250	>10	>10	>10	2.1	1.2	0.9	1.5	0.8	0.6
1	25	500	>10	>10	7.8	1.7	0.8	0.6	1.1	0.5	0.3
1	25	750	>10	8.2	5.7	1.4	0.6	0.4	0.9	0.4	0.2
1	25	1000	>10	6.5	4.5	1.2	0.5	0.3	0.7	0.3	0.2
1	30	130	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.7
1	30	250	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
1	30	500	>10	9.5	6.7	1.5	0.7	0.5	1.0	0.4	0.3
1	30	750	>10	7.0	4.9	1.2	0.5	0.3	0.8	0.3	0.2
1	30	1000	>10	5.6	3.8	1.0	0.4	0.3	0.7	0.2	0.2
1.5	10	130	>10	>10	>10	2.3	1.3	1.0	1.6	0.9	0.7
1.5	10	250	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
1.5	10	500	>10	>10	7.9	1.6	0.7	0.5	1.1	0.5	0.3
1.5	10	750	>10	8.1	5.7	1.2	0.5	0.4	0.8	0.3	0.2
1.5	10	1000	>10	6.4	4.4	1.0	0.4	0.3	0.7	0.3	0.2
1.5	15	130	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1.5	15	250	>10	>10	9.7	1.8	0.9	0.6	1.3	0.6	0.4
1.5	15	500	>10	8.5	6.0	1.3	0.5	0.4	0.9	0.4	0.3
1.5	15	750	>10	6.1	4.2	1.0	0.4	0.3	0.7	0.3	0.2
1.5	15	1000	>10	4.7	3.2	0.8	0.3	0.2	0.6	0.2	0.1
1.5	20	130	>10	>10	>10	2.0	1.1	0.8	1.5	0.7	0.6
1.5	20	250	>10	>10	8.5	1.7	0.8	0.5	1.1	0.5	0.4
1.5	20	500	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
1.5	20	750	>10	5.0	3.4	0.9	0.3	0.2	0.6	0.2	0.1
1.5	20	1000	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
1.5	25	130	>10	>10	>10	1.9	1.0	0.7	1.4	0.7	0.5
1.5	25	250	>10	>10	7.5	1.5	0.7	0.5	1.1	0.5	0.3
1.5	25	500	>10	6.3	4.4	1.0	0.4	0.3	0.7	0.3	0.2
1.5	25	750	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
1.5	25	1000	9.2	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
1.5	30	130	>10	>10	9.8	1.8	0.9	0.7	1.3	0.6	0.4
1.5	30	250	>10	9.5	6.8	1.4	0.6	0.4	1.0	0.4	0.3

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1.5	30	500	>10	5.5	3.8	0.9	0.4	0.2	0.6	0.2	0.2
1.5	30	750	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
1.5	30	1000	8.2	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	10	130	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
2	10	250	>10	>10	8.2	1.6	0.7	0.5	1.1	0.5	0.3
2	10	500	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
2	10	750	>10	5.2	3.6	0.9	0.3	0.2	0.6	0.2	0.1
2	10	1000	>10	4.0	2.8	0.7	0.3	0.2	0.5	0.2	0.1
2	15	130	>10	>10	9.5	1.8	0.9	0.6	1.3	0.6	0.4
2	15	250	>10	8.9	6.3	1.4	0.6	0.4	0.9	0.4	0.3
2	15	500	>10	5.3	3.7	0.9	0.3	0.2	0.6	0.2	0.2
2	15	750	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
2	15	1000	8.3	2.9	2.0	0.5	0.2	0.1	0.4	0.1	0.1
2	20	130	>10	>10	8.1	1.6	0.8	0.5	1.1	0.5	0.4
2	20	250	>10	7.3	5.1	1.2	0.5	0.3	0.8	0.3	0.2
2	20	500	>10	4.2	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2	20	750	8.4	2.9	2.0	0.6	0.2	0.1	0.4	0.1	0.1
2	20	1000	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2	25	130	>10	>10	7.2	1.5	0.7	0.5	1.1	0.5	0.3
2	25	250	>10	6.4	4.4	1.1	0.4	0.3	0.7	0.3	0.2
2	25	500	>10	3.6	2.4	0.7	0.2	0.2	0.5	0.2	0.1
2	25	750	7.2	2.5	1.7	0.5	0.2	0.1	0.3	0.1	0.1
2	25	1000	5.6	1.9	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2	30	130	>10	9.0	6.4	1.4	0.6	0.4	1.0	0.4	0.3
2	30	250	>10	5.6	3.9	1.0	0.4	0.3	0.7	0.2	0.2
2	30	500	8.9	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2	30	750	6.4	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
2	30	1000	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	>10	9.9	1.8	0.9	0.7	1.3	0.6	0.4
2.5	10	250	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
2.5	10	500	>10	5.8	4.0	1.0	0.4	0.3	0.6	0.2	0.2
2.5	10	750	>10	4.1	2.8	0.7	0.3	0.2	0.5	0.2	0.1
2.5	10	1000	9.1	3.2	2.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	130	>10	>10	8.0	1.6	0.7	0.5	1.1	0.5	0.3
2.5	15	250	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
2.5	15	500	>10	4.2	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2.5	15	750	8.5	2.9	2.0	0.5	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	6.7	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	20	130	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
2.5	20	250	>10	5.8	4.0	1.0	0.4	0.3	0.7	0.3	0.2
2.5	20	500	9.3	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	20	750	6.8	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0
2.5	25	130	>10	8.1	5.7	1.3	0.5	0.4	0.9	0.4	0.3
2.5	25	250	>10	4.9	3.4	0.9	0.3	0.2	0.6	0.2	0.1
2.5	25	500	7.9	2.7	1.8	0.5	0.2	0.1	0.4	0.1	0.1
2.5	25	750	5.7	1.9	1.3	0.4	0.1	0.1	0.3	0.1	0.1
2.5	25	1000	4.4	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	130	>10	7.2	5.1	1.2	0.5	0.3	0.8	0.3	0.2
2.5	30	250	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2.5	30	500	7.0	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
2.5	30	750	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	3.8	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	>10	8.4	1.7	0.8	0.6	1.1	0.5	0.4
3	10	250	>10	7.5	5.3	1.2	0.5	0.3	0.8	0.3	0.2
3	10	500	>10	4.4	3.0	0.8	0.3	0.2	0.5	0.2	0.1
3	10	750	8.6	3.0	2.0	0.6	0.2	0.1	0.4	0.1	0.1
3	10	1000	6.8	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	130	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
3	15	250	>10	5.7	3.9	1.0	0.4	0.3	0.7	0.2	0.2
3	15	500	9.0	3.2	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	6.4	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	1000	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	130	>10	7.7	5.4	1.2	0.5	0.4	0.8	0.3	0.2
3	20	250	>10	4.6	3.1	0.8	0.3	0.2	0.5	0.2	0.1
3	20	500	7.3	2.5	1.7	0.5	0.2	0.1	0.3	0.1	0.1
3	20	750	5.1	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	3.9	1.3	0.8	0.3	0.1	0.1	0.2	0.1	0.0
3	25	130	>10	6.6	4.6	1.1	0.4	0.3	0.8	0.3	0.2
3	25	250	>10	3.9	2.6	0.7	0.2	0.2	0.5	0.2	0.1
3	25	500	6.1	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	25	750	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	3.3	1.0	0.7	0.2	0.1	0.0	0.1	0.0	0.0
3	30	130	>10	5.8	4.0	1.0	0.4	0.3	0.7	0.3	0.2
3	30	250	9.3	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
3	30	500	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3	30	750	3.7	1.2	0.8	0.2	0.1	0.0	0.2	0.0	0.0
3	30	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	7.2	5.1	1.3	0.5	0.4	0.9	0.4	0.3
3.5	10	250	>10	4.7	3.2	0.9	0.3	0.2	0.6	0.2	0.2
3.5	10	500	7.3	2.5	1.7	0.5	0.2	0.1	0.4	0.1	0.1
3.5	10	750	5.3	1.7	1.2	0.4	0.1	0.1	0.2	0.1	0.1
3.5	10	1000	4.5	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	130	>10	6.1	4.2	1.1	0.4	0.3	0.8	0.3	0.2
3.5	15	250	>10	3.7	2.5	0.7	0.3	0.2	0.5	0.2	0.1
3.5	15	500	5.9	2.0	1.3	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	4.2	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	130	>10	5.2	3.6	1.0	0.4	0.2	0.7	0.3	0.2
3.5	20	250	8.9	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	20	500	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	3.5	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	130	>10	4.6	3.1	0.9	0.3	0.2	0.6	0.2	0.1
3.5	25	250	7.7	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
3.5	25	500	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	25	750	2.9	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	2.4	0.7	0.5	0.2	0.0	0.0	0.1	0.0	0.0
3.5	30	130	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3.5	30	250	6.8	2.3	1.6	0.5	0.2	0.1	0.3	0.1	0.1
3.5	30	500	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3.5	30	750	2.6	0.8	0.5	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	1000	2.0	0.6	0.4	0.1	0.0	0.0	0.1	0.0	0.0

9.4.2 AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 60s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.2	0.8	0.6	10.6	0.8	0.6
0.5	20	500	9.8	0.7	0.5	9.4	0.7	0.5
0.5	30	250	9.9	0.7	0.5	9.7	0.7	0.5
0.5	30	500	9.3	0.7	0.5	8.2	0.6	0.5
1	20	250	9.8	0.7	0.5	9.4	0.7	0.5
1	20	500	9.1	0.7	0.5	7.6	0.5	0.4
1	30	250	9.3	0.7	0.5	8.2	0.6	0.4
1	30	500	8.4	0.6	0.4	6.3	0.5	0.3
1.5	20	250	8.9	0.6	0.5	7.2	0.5	0.3
1.5	20	500	7.7	0.5	0.4	5.2	0.3	0.2
1.5	30	250	8.4	0.6	0.4	6.3	0.4	0.3
1.5	30	500	7.0	0.5	0.3	4.2	0.3	0.2
2	20	250	7.7	0.6	0.4	5.2	0.4	0.2
2	20	500	6.2	0.4	0.3	3.4	0.2	0.2
2	30	250	7.0	0.5	0.3	4.3	0.3	0.2
2	30	500	5.3	0.4	0.3	2.6	0.2	0.1
2.5	20	250	7.1	0.5	0.4	4.4	0.3	0.2
2.5	20	500	5.4	0.4	0.3	2.7	0.2	0.1
2.5	30	250	6.2	0.4	0.3	3.4	0.2	0.2
2.5	30	500	4.5	0.3	0.2	2.0	0.1	0.1
3	20	250	6.4	0.4	0.3	3.6	0.2	0.2
3	20	500	4.6	0.3	0.2	2.1	0.1	0.1
3	30	250	5.4	0.4	0.3	2.7	0.2	0.1
3	30	500	3.7	0.2	0.2	1.6	0.1	0.1
3.5	20	250	5.3	0.4	0.3	2.6	0.2	0.1
3.5	20	500	3.5	0.2	0.2	1.5	0.1	0.1
3.5	30	250	4.4	0.3	0.2	2.0	0.1	0.1
3.5	30	500	2.8	0.2	0.1	1.1	0.1	0.0

9.4.3 AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 30s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.2	0.8	0.6	10.6	0.8	0.6
0.5	20	500	9.8	0.7	0.5	9.4	0.7	0.5
0.5	30	250	9.9	0.7	0.5	9.7	0.7	0.5
0.5	30	500	9.4	0.7	0.5	8.2	0.6	0.5
1	20	250	9.8	0.7	0.5	9.4	0.7	0.5
1	20	500	9.1	0.7	0.5	7.6	0.5	0.4
1	30	250	9.4	0.7	0.5	8.2	0.6	0.4
1	30	500	8.5	0.6	0.4	6.3	0.5	0.3
1.5	20	250	9.0	0.6	0.5	7.3	0.5	0.3
1.5	20	500	7.8	0.6	0.4	5.2	0.3	0.2
1.5	30	250	8.5	0.6	0.4	6.3	0.4	0.3
1.5	30	500	7.1	0.5	0.3	4.3	0.3	0.2
2	20	250	7.8	0.6	0.4	5.2	0.4	0.2
2	20	500	6.3	0.4	0.3	3.4	0.2	0.2
2	30	250	7.2	0.5	0.4	4.3	0.3	0.2
2	30	500	5.5	0.4	0.3	2.7	0.2	0.1
2.5	20	250	7.3	0.5	0.4	4.4	0.3	0.2
2.5	20	500	5.6	0.4	0.3	2.8	0.2	0.1
2.5	30	250	6.4	0.4	0.3	3.5	0.2	0.2
2.5	30	500	4.6	0.3	0.2	2.1	0.1	0.1
3	20	250	6.6	0.5	0.3	3.7	0.2	0.2
3	20	500	4.8	0.3	0.2	2.2	0.1	0.1
3	30	250	5.6	0.4	0.3	2.8	0.2	0.1
3	30	500	3.8	0.3	0.2	1.6	0.1	0.1
3.5	20	250	5.4	0.4	0.3	2.6	0.2	0.1
3.5	20	500	3.7	0.3	0.2	1.5	0.1	0.1
3.5	30	250	4.6	0.3	0.2	2.0	0.1	0.1
3.5	30	500	2.9	0.2	0.1	1.1	0.1	0.0

9.4.4 AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 60s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.3	0.8	0.6	10.8	0.8	0.6
0.5	20	500	9.7	0.7	0.5	9.3	0.7	0.5
0.5	30	250	9.8	0.7	0.5	9.6	0.7	0.5
0.5	30	500	9.0	0.7	0.5	8.0	0.6	0.4
1	20	250	9.7	0.7	0.5	9.3	0.7	0.5
1	20	500	8.6	0.6	0.4	7.3	0.5	0.3
1	30	250	9.0	0.7	0.5	8.0	0.6	0.4
1	30	500	7.6	0.6	0.4	5.9	0.4	0.3
1.5	20	250	8.3	0.6	0.4	6.9	0.5	0.3
1.5	20	500	6.7	0.5	0.3	4.8	0.3	0.2
1.5	30	250	7.6	0.5	0.4	5.9	0.4	0.3
1.5	30	500	5.8	0.4	0.3	3.9	0.3	0.2
2	20	250	6.7	0.5	0.3	4.8	0.3	0.2
2	20	500	5.0	0.3	0.2	3.1	0.2	0.1
2	30	250	5.9	0.4	0.3	3.9	0.3	0.2
2	30	500	4.1	0.3	0.2	2.4	0.2	0.1
2.5	20	250	6.0	0.4	0.3	4.0	0.3	0.2
2.5	20	500	4.2	0.3	0.2	2.5	0.2	0.1
2.5	30	250	5.0	0.3	0.2	3.1	0.2	0.1
2.5	30	500	3.3	0.2	0.2	1.8	0.1	0.1
3	20	250	5.2	0.4	0.2	3.3	0.2	0.1
3	20	500	3.4	0.2	0.2	1.9	0.1	0.1
3	30	250	4.2	0.3	0.2	2.5	0.2	0.1
3	30	500	2.6	0.2	0.1	1.4	0.1	0.1
3.5	20	250	4.0	0.3	0.2	2.3	0.2	0.1
3.5	20	500	2.5	0.2	0.1	1.3	0.1	0.1
3.5	30	250	3.3	0.2	0.1	1.8	0.1	0.1
3.5	30	500	1.9	0.1	0.1	1.0	0.1	0.0

9.4.5 AutoStim Feature Enabled (7 AutoStims/Hour, AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 30s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.2	0.8	0.6	10.7	0.8	0.6
0.5	20	500	9.8	0.7	0.5	9.4	0.7	0.5
0.5	30	250	9.9	0.7	0.5	9.7	0.7	0.5
0.5	30	500	9.2	0.7	0.5	8.1	0.6	0.5
1	20	250	9.8	0.7	0.5	9.4	0.7	0.5
1	20	500	8.9	0.7	0.5	7.5	0.5	0.4
1	30	250	9.3	0.7	0.5	8.2	0.6	0.4
1	30	500	8.2	0.6	0.4	6.2	0.4	0.3
1.5	20	250	8.8	0.6	0.4	7.1	0.5	0.3
1.5	20	500	7.4	0.5	0.4	5.1	0.3	0.2
1.5	30	250	8.2	0.6	0.4	6.2	0.4	0.3
1.5	30	500	6.6	0.5	0.3	4.1	0.3	0.2
2	20	250	7.5	0.5	0.4	5.1	0.3	0.2
2	20	500	5.8	0.4	0.3	3.3	0.2	0.1
2	30	250	6.7	0.5	0.3	4.2	0.3	0.2
2	30	500	4.9	0.3	0.2	2.6	0.2	0.1
2.5	20	250	6.8	0.5	0.3	4.3	0.3	0.2
2.5	20	500	5.1	0.3	0.2	2.7	0.2	0.1
2.5	30	250	5.9	0.4	0.3	3.4	0.2	0.2
2.5	30	500	4.1	0.3	0.2	2.0	0.1	0.1
3	20	250	6.1	0.4	0.3	3.5	0.2	0.2
3	20	500	4.3	0.3	0.2	2.1	0.1	0.1
3	30	250	5.1	0.3	0.2	2.7	0.2	0.1
3	30	500	3.3	0.2	0.2	1.5	0.1	0.1
3.5	20	250	4.9	0.3	0.2	2.5	0.2	0.1
3.5	20	500	3.2	0.2	0.2	1.4	0.1	0.1
3.5	30	250	4.1	0.3	0.2	2.0	0.1	0.1
3.5	30	500	2.5	0.2	0.1	1.1	0.1	0.0

9.4.6 AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 60s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.5	0.8	0.6	10.9	0.8	0.6
0.5	20	500	9.5	0.7	0.5	9.2	0.7	0.5
0.5	30	250	9.7	0.7	0.5	9.6	0.7	0.5
0.5	30	500	8.5	0.6	0.5	7.7	0.6	0.4
1	20	250	9.5	0.7	0.5	9.2	0.7	0.4
1	20	500	8.0	0.6	0.4	7.0	0.5	0.3
1	30	250	8.5	0.6	0.4	7.7	0.6	0.4
1	30	500	6.8	0.5	0.3	5.5	0.4	0.3
1.5	20	250	7.7	0.5	0.4	6.6	0.4	0.3
1.5	20	500	5.7	0.4	0.3	4.4	0.3	0.2
1.5	30	250	6.8	0.5	0.3	5.5	0.4	0.2
1.5	30	500	4.8	0.3	0.2	3.5	0.2	0.2
2	20	250	5.8	0.4	0.3	4.4	0.3	0.2
2	20	500	3.9	0.3	0.2	2.8	0.2	0.1
2	30	250	4.8	0.3	0.2	3.5	0.2	0.2
2	30	500	3.1	0.2	0.1	2.1	0.1	0.1
2.5	20	250	5.0	0.3	0.2	3.7	0.2	0.2
2.5	20	500	3.2	0.2	0.1	2.2	0.1	0.1
2.5	30	250	4.0	0.3	0.2	2.8	0.2	0.1
2.5	30	500	2.5	0.2	0.1	1.6	0.1	0.1
3	20	250	4.2	0.3	0.2	3.0	0.2	0.1
3	20	500	2.6	0.2	0.1	1.7	0.1	0.1
3	30	250	3.2	0.2	0.1	2.2	0.1	0.1
3	30	500	1.9	0.1	0.1	1.2	0.1	0.1
3.5	20	250	3.1	0.2	0.1	2.1	0.1	0.1
3.5	20	500	1.8	0.1	0.1	1.1	0.1	0.1
3.5	30	250	2.4	0.2	0.1	1.6	0.1	0.1
3.5	30	500	1.3	0.1	0.1	0.8	0.1	0.0

9.4.7 AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 30s) Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	10.3	0.8	0.6	10.7	0.8	0.6
0.5	20	500	9.7	0.7	0.5	9.3	0.7	0.5
0.5	30	250	9.8	0.7	0.5	9.7	0.7	0.5
0.5	30	500	9.1	0.7	0.5	8.0	0.6	0.4
1	20	250	9.7	0.7	0.5	9.3	0.7	0.5
1	20	500	8.7	0.6	0.4	7.4	0.5	0.4
1	30	250	9.1	0.7	0.5	8.1	0.6	0.4
1	30	500	7.8	0.6	0.4	6.0	0.4	0.3
1.5	20	250	8.5	0.6	0.4	7.0	0.5	0.3
1.5	20	500	7.0	0.5	0.3	4.9	0.3	0.2
1.5	30	250	7.8	0.5	0.4	6.0	0.4	0.3
1.5	30	500	6.1	0.4	0.3	4.0	0.3	0.2
2	20	250	7.0	0.5	0.3	4.9	0.3	0.2
2	20	500	5.3	0.4	0.3	3.2	0.2	0.1
2	30	250	6.2	0.4	0.3	4.0	0.3	0.2
2	30	500	4.4	0.3	0.2	2.4	0.2	0.1
2.5	20	250	6.3	0.4	0.3	4.1	0.3	0.2
2.5	20	500	4.5	0.3	0.2	2.5	0.2	0.1
2.5	30	250	5.3	0.4	0.3	3.2	0.2	0.1
2.5	30	500	3.6	0.2	0.2	1.9	0.1	0.1
3	20	250	5.5	0.4	0.3	3.4	0.2	0.1
3	20	500	3.7	0.2	0.2	2.0	0.1	0.1
3	30	250	4.5	0.3	0.2	2.5	0.2	0.1
3	30	500	2.8	0.2	0.1	1.4	0.1	0.1
3.5	20	250	4.3	0.3	0.2	2.4	0.2	0.1
3.5	20	500	2.7	0.2	0.1	1.3	0.1	0.1
3.5	30	250	3.5	0.2	0.2	1.9	0.1	0.1
3.5	30	500	2.1	0.1	0.1	1.0	0.1	0.0

9.5 Appendix E — Model 1000/1000-D Battery Longevity and Programmed Setting Choices

9.5.1 AutoStim Feature Disabled

Parameters at 3kOhms			AutoStim Feature Disabled Normal Mode Duty Cycle								
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)			51% (60s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	20	250	11.9	1.2	1.2	6.1	0.6	0.6	4.6	0.5	0.5
0.5	20	500	11.8	1.2	1.2	6.0	0.6	0.6	4.5	0.5	0.5
0.5	30	250	10.2	1.0	1.0	4.7	0.5	0.5	3.5	0.4	0.4
0.5	30	500	10.1	1.0	1.0	4.6	0.5	0.5	3.4	0.3	0.3
1	20	250	11.7	1.2	1.2	5.9	0.6	0.6	4.5	0.5	0.4
1	20	500	11.6	1.2	1.1	5.8	0.6	0.5	4.4	0.4	0.4
1	30	250	10.0	1.0	1.0	4.5	0.5	0.5	3.3	0.3	0.3
1	30	500	9.9	1.0	1.0	4.4	0.4	0.4	3.2	0.3	0.3
1.5	20	250	11.4	1.1	1.1	5.7	0.6	0.5	4.2	0.4	0.4
1.5	20	500	9.4	0.9	0.8	4.1	0.4	0.3	3.0	0.3	0.2
1.5	30	250	9.8	1.0	0.9	4.4	0.4	0.4	3.2	0.3	0.3
1.5	30	500	7.7	0.7	0.7	3.1	0.3	0.2	2.2	0.2	0.2
2	20	250	9.7	0.9	0.8	4.3	0.4	0.3	3.2	0.3	0.2
2	20	500	7.2	0.7	0.6	2.8	0.3	0.2	2.0	0.2	0.2
2	30	250	8.2	0.8	0.7	3.3	0.3	0.3	2.4	0.2	0.2
2	30	500	5.6	0.5	0.5	2.0	0.2	0.2	1.4	0.1	0.1
2.5	20	250	7.9	0.7	0.7	3.2	0.3	0.2	2.3	0.2	0.2
2.5	20	500	5.5	0.5	0.4	1.9	0.2	0.1	1.4	0.1	0.1
2.5	30	250	6.5	0.6	0.5	2.4	0.2	0.2	1.7	0.2	0.1
2.5	30	500	4.2	0.4	0.3	1.4	0.1	0.1	1.0	0.1	0.1
3	20	250	6.4	0.6	0.5	2.4	0.2	0.2	1.7	0.2	0.1
3	20	500	4.2	0.4	0.3	1.4	0.1	0.1	1.0	0.1	0.1
3	30	250	5.1	0.5	0.4	1.8	0.2	0.1	1.2	0.1	0.1
3	30	500	3.1	0.3	0.2	1.0	0.1	0.1	0.7	0.1	0.1
3.5	20	250	5.2	0.5	0.4	1.8	0.2	0.1	1.3	0.1	0.1
3.5	20	500	3.2	0.3	0.2	1.0	0.1	0.1	0.7	0.1	0.1
3.5	30	250	4.0	0.4	0.3	1.3	0.1	0.1	0.9	0.1	0.1
3.5	30	500	2.3	0.2	0.2	0.7	0.1	0.1	0.5	0.0	0.0

9.5.2 AutoStim Feature Enabled (1 AutoStims/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 60s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	7.3	0.7	0.7	4.9	0.5	0.5
0.5	20	500	7.2	0.7	0.7	4.8	0.5	0.5
0.5	30	250	6.5	0.7	0.7	3.9	0.4	0.4
0.5	30	500	6.5	0.7	0.7	3.9	0.4	0.4
1	20	250	7.2	0.7	0.7	4.8	0.5	0.5
1	20	500	7.1	0.7	0.7	4.7	0.5	0.4
1	30	250	6.4	0.7	0.7	3.8	0.4	0.4
1	30	500	6.4	0.6	0.6	3.7	0.4	0.4
1.5	20	250	7.1	0.7	0.7	4.6	0.5	0.4
1.5	20	500	6.1	0.6	0.6	3.5	0.3	0.3
1.5	30	250	6.3	0.6	0.6	3.7	0.4	0.3
1.5	30	500	5.3	0.5	0.5	2.7	0.3	0.2
2	20	250	6.3	0.6	0.6	3.7	0.3	0.3
2	20	500	5.0	0.5	0.4	2.5	0.2	0.2
2	30	250	5.5	0.5	0.5	2.9	0.3	0.2
2	30	500	4.1	0.4	0.3	1.8	0.2	0.1
2.5	20	250	5.4	0.5	0.5	2.8	0.3	0.2
2.5	20	500	4.0	0.4	0.3	1.8	0.2	0.1
2.5	30	250	4.6	0.4	0.4	2.2	0.2	0.2
2.5	30	500	3.2	0.3	0.3	1.3	0.1	0.1
3	20	250	4.6	0.4	0.4	2.1	0.2	0.2
3	20	500	3.2	0.3	0.3	1.3	0.1	0.1
3	30	250	3.8	0.4	0.3	1.6	0.1	0.1
3	30	500	2.5	0.2	0.2	0.9	0.1	0.1
3.5	20	250	3.8	0.4	0.3	1.7	0.2	0.1
3.5	20	500	2.5	0.2	0.2	1.0	0.1	0.1
3.5	30	250	3.1	0.3	0.3	1.2	0.1	0.1
3.5	30	500	1.9	0.2	0.1	0.7	0.1	0.1

*Longevity values with Prone Detection ON vary by no more than 4%.

9.5.3 AutoStim Feature Enabled (1 AutoStims/Hour and AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (1 AutoStim/Hour and AutoStim ON time 30s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	7.4	0.8	0.8	4.9	0.5	0.5
0.5	20	500	7.3	0.7	0.8	4.9	0.5	0.5
0.5	30	250	6.7	0.7	0.7	4.0	0.4	0.4
0.5	30	500	6.6	0.7	0.7	3.9	0.4	0.4
1	20	250	7.3	0.7	0.7	4.8	0.5	0.5
1	20	500	7.3	0.7	0.7	4.8	0.5	0.5
1	30	250	6.6	0.7	0.7	3.9	0.4	0.4
1	30	500	6.5	0.7	0.6	3.8	0.4	0.4
1.5	20	250	7.2	0.7	0.7	4.7	0.5	0.4
1.5	20	500	6.3	0.6	0.6	3.5	0.3	0.3
1.5	30	250	6.5	0.7	0.6	3.7	0.4	0.3
1.5	30	500	5.5	0.5	0.5	2.7	0.3	0.2
2	20	250	6.5	0.6	0.6	3.7	0.3	0.3
2	20	500	5.2	0.5	0.5	2.5	0.2	0.2
2	30	250	5.7	0.6	0.5	2.9	0.3	0.2
2	30	500	4.3	0.4	0.4	1.9	0.2	0.1
2.5	20	250	5.6	0.5	0.5	2.8	0.3	0.2
2.5	20	500	4.2	0.4	0.4	1.8	0.2	0.1
2.5	30	250	4.8	0.5	0.4	2.2	0.2	0.2
2.5	30	500	3.4	0.3	0.3	1.3	0.1	0.1
3	20	250	4.8	0.4	0.4	2.2	0.2	0.2
3	20	500	3.4	0.3	0.3	1.3	0.1	0.1
3	30	250	4.0	0.4	0.3	1.7	0.2	0.1
3	30	500	2.6	0.2	0.2	0.9	0.1	0.1
3.5	20	250	4.0	0.4	0.3	1.7	0.2	0.1
3.5	20	500	2.7	0.2	0.2	1.0	0.1	0.1
3.5	30	250	3.2	0.3	0.3	1.3	0.1	0.1
3.5	30	500	2.0	0.2	0.2	0.7	0.1	0.1

*Longevity values with Prone Detection ON vary by no more than 5%.

9.5.4 AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 60s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	6.3	0.6	0.7	4.6	0.5	0.5
0.5	20	500	6.3	0.6	0.6	4.5	0.5	0.5
0.5	30	250	5.5	0.6	0.6	3.6	0.4	0.4
0.5	30	500	5.4	0.5	0.6	3.5	0.4	0.4
1	20	250	6.3	0.6	0.6	4.5	0.5	0.5
1	20	500	6.2	0.6	0.6	4.4	0.4	0.4
1	30	250	5.4	0.5	0.5	3.5	0.4	0.4
1	30	500	5.3	0.5	0.5	3.4	0.3	0.3
1.5	20	250	6.1	0.6	0.6	4.3	0.4	0.4
1.5	20	500	5.0	0.5	0.4	3.2	0.3	0.3
1.5	30	250	5.2	0.5	0.5	3.4	0.3	0.3
1.5	30	500	4.1	0.4	0.4	2.4	0.2	0.2
2	20	250	5.2	0.5	0.4	3.4	0.3	0.3
2	20	500	3.8	0.4	0.3	2.2	0.2	0.2
2	30	250	4.4	0.4	0.4	2.6	0.2	0.2
2	30	500	3.0	0.3	0.2	1.6	0.1	0.1
2.5	20	250	4.2	0.4	0.4	2.5	0.2	0.2
2.5	20	500	2.9	0.3	0.2	1.6	0.1	0.1
2.5	30	250	3.5	0.3	0.3	1.9	0.2	0.2
2.5	30	500	2.2	0.2	0.2	1.1	0.1	0.1
3	20	250	3.4	0.3	0.3	1.9	0.2	0.1
3	20	500	2.2	0.2	0.2	1.2	0.1	0.1
3	30	250	2.7	0.3	0.2	1.5	0.1	0.1
3	30	500	1.7	0.1	0.1	0.8	0.1	0.1
3.5	20	250	2.8	0.3	0.2	1.5	0.1	0.1
3.5	20	500	1.7	0.2	0.1	0.8	0.1	0.1
3.5	30	250	2.1	0.2	0.2	1.1	0.1	0.1
3.5	30	500	1.2	0.1	0.1	0.6	0.1	0.0

*Longevity values with Prone Detection ON vary by no more than 4%.

9.5.5 AutoStim Feature Enabled (7 AutoStims/Hour, AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (7 AutoStims/Hour and AutoStim ON time 30s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	7.0	0.7	0.7	4.8	0.5	0.5
0.5	20	500	7.0	0.7	0.7	4.7	0.5	0.5
0.5	30	250	6.2	0.6	0.6	3.9	0.4	0.4
0.5	30	500	6.2	0.6	0.6	3.8	0.4	0.4
1	20	250	6.9	0.7	0.7	4.7	0.5	0.5
1	20	500	6.9	0.7	0.7	4.6	0.5	0.4
1	30	250	6.1	0.6	0.6	3.7	0.4	0.4
1	30	500	6.1	0.6	0.6	3.7	0.4	0.3
1.5	20	250	6.8	0.7	0.7	4.5	0.5	0.4
1.5	20	500	5.8	0.6	0.5	3.4	0.3	0.3
1.5	30	250	6.0	0.6	0.6	3.6	0.4	0.3
1.5	30	500	5.0	0.5	0.4	2.6	0.2	0.2
2	20	250	6.0	0.6	0.5	3.6	0.3	0.3
2	20	500	4.7	0.4	0.4	2.4	0.2	0.2
2	30	250	5.2	0.5	0.5	2.8	0.36	0.2
2	30	500	3.8	0.4	0.3	1.8	0.2	0.1
2.5	20	250	5.1	0.5	0.4	2.7	0.3	0.2
2.5	20	500	3.7	0.3	0.3	1.7	0.2	0.1
2.5	30	250	4.3	0.4	0.4	2.1	0.2	0.2
2.5	30	500	2.9	0.3	0.2	1.3	0.1	0.1
3	20	250	4.2	0.4	0.4	2.1	0.2	0.2
3	20	500	2.9	0.3	0.2	1.3	0.1	0.1
3	30	250	3.5	0.3	0.3	1.6	0.1	0.1
3	30	500	2.2	0.2	0.2	0.9	0.1	0.1
3.5	20	250	3.5	0.3	0.3	1.6	0.1	0.1
3.5	20	500	2.3	0.2	0.2	0.9	0.1	0.1
3.5	30	250	2.8	0.3	0.2	1.2	0.1	0.1
3.5	30	500	1.7	0.2	0.1	0.7	0.1	0.0

*Longevity values with Prone Detection ON vary by no more than 5%.

9.5.6 AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 60 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 60s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	5.4	0.6	0.6	4.2	0.4	0.4
0.5	20	500	5.4	0.5	0.6	4.1	0.4	0.4
0.5	30	250	4.5	0.5	0.5	3.3	0.3	0.3
0.5	30	500	4.4	0.4	0.5	3.2	0.3	0.3
1	20	250	5.3	0.5	0.5	4.1	0.4	0.4
1	20	500	5.3	0.5	0.5	4.0	0.4	0.4
1	30	250	4.4	0.4	0.4	3.2	0.3	0.3
1	30	500	4.3	0.4	0.4	3.1	0.3	0.3
1.5	20	250	5.2	0.5	0.5	3.9	0.4	0.4
1.5	20	500	4.0	0.4	0.3	2.9	0.3	0.2
1.5	30	250	4.3	0.4	0.4	3.1	0.3	0.3
1.5	30	500	3.2	0.3	0.3	2.2	0.2	0.2
2	20	250	4.2	0.4	0.4	3.0	0.3	0.2
2	20	500	2.9	0.3	0.2	2.0	0.2	0.2
2	30	250	3.4	0.3	0.3	2.3	0.2	0.2
2	30	500	2.2	0.2	0.2	1.4	0.1	0.1
2.5	20	250	3.3	0.3	0.3	2.2	0.2	0.2
2.5	20	500	2.1	0.2	0.2	1.4	0.1	0.1
2.5	30	250	2.6	0.2	0.2	1.7	0.2	0.1
2.5	30	500	1.6	0.1	0.1	1.0	0.1	0.1
3	20	250	2.6	0.2	0.2	1.7	0.2	0.1
3	20	500	1.6	0.1	0.1	1.0	0.1	0.1
3	30	250	2.0	0.2	0.2	1.3	0.1	0.1
3	30	500	1.1	0.1	0.1	0.7	0.1	0.1
3.5	20	250	2.0	0.2	0.2	1.3	0.1	0.1
3.5	20	500	1.2	0.1	0.1	0.7	0.1	0.1
3.5	30	250	1.5	0.1	0.1	0.9	0.1	0.1
3.5	30	500	0.8	0.1	0.1	0.5	0.0	0.0

*Longevity values with Prone Detection ON vary by no more than 4%.

9.5.7 AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 30 seconds)

Parameters at 3kOhms			AutoStim Feature Enabled (15 AutoStims/Hour and AutoStim ON time 30s)* Normal Mode Duty Cycle					
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years
0.5	20	250	6.6	0.7	0.7	4.6	0.5	0.5
0.5	20	500	6.5	0.7	0.7	4.6	0.5	0.5
0.5	30	250	5.7	0.6	0.6	3.7	0.4	0.4
0.5	30	500	5.7	0.6	0.6	3.6	0.4	0.4
1	20	250	6.5	0.7	0.7	4.6	0.5	0.5
1	20	500	6.5	0.6	0.6	4.5	0.4	0.4
1	30	250	5.6	0.6	0.6	3.6	0.4	0.4
1	30	500	5.5	0.6	0.5	3.5	0.4	0.3
1.5	20	250	6.4	0.6	0.6	4.4	0.4	0.4
1.5	20	500	5.3	0.5	0.5	3.3	0.3	0.3
1.5	30	250	5.5	0.6	0.5	3.5	0.4	0.3
1.5	30	500	4.4	0.4	0.4	2.5	0.2	0.2
2	20	250	5.5	0.5	0.5	3.4	0.3	0.3
2	20	500	4.1	0.4	0.3	2.3	0.2	0.2
2	30	250	4.7	0.4	0.4	2.7	0.3	0.2
2	30	500	3.3	0.3	0.3	1.7	0.2	0.1
2.5	20	250	4.5	0.4	0.4	2.6	0.2	0.2
2.5	20	500	3.2	0.3	0.3	1.6	0.1	0.1
2.5	30	250	3.7	0.4	0.3	2.0	0.2	0.2
2.5	30	500	2.4	0.2	0.2	1.2	0.1	0.1
3	20	250	3.7	0.3	0.3	2.0	0.2	0.2
3	20	500	2.5	0.2	0.2	1.2	0.1	0.1
3	30	250	3.0	0.3	0.2	1.5	0.1	0.1
3	30	500	1.8	0.2	0.1	0.8	0.1	0.1
3.5	20	250	3.0	0.3	0.2	1.5	0.1	0.1
3.5	20	500	1.9	0.2	0.1	0.9	0.1	0.1
3.5	30	250	2.4	0.2	0.2	1.1	0.1	0.1
3.5	30	500	1.4	0.1	0.1	0.6	0.1	0.0

*Longevity values with Prone Detection ON vary by no more than 5%.

9.6 Appendix F — Mean Sensitivity and Potential False Positive Rates per Threshold for AutoStim Setting (Models 106 and 1000/1000-D)

The following table is applicable for generators with the AutoStim feature only and supplements the "Receiver Operating Characteristic (ROC) Curve for Tachycardia Detection Associated with Seizures" figure within the *model specific Technical Information* chapter.

This table lists the mean values and 95% confidence intervals (CI) from the E36 and E37 clinical study performance data.

Threshold for AutoStim	Mean Sensitivity (%) (95% CI)[a]			Potential False Positives per Hour (95% CI)[a]
	Ictal Tachycardia Seizures Only (—♦—) n=11 pts, 28 sz	Seizures ≥ 20% Heart Rate Change (- -●- -) n=25 pts, 82 sz	All Patients (pts), All Seizures (sz) (—■—) n=34 pts, 170 sz	Applies to All Categories n=50 pts, 4516 hrs
70% Threshold	60.7 (40.0, 81.8)	26.8 (14.2, 42.9)	18.8 (10.5, 34.4)	0.4 (0.3, 0.5)
60% Threshold	67.9 (46.9, 88.0)	39.0 (23.8, 53.9)	27.1 (12.9, 41.0)	0.6 (0.5, 0.8)
50% Threshold	85.7 (70.4, 96.0)	56.1 (38.1, 73.0)	41.2 (20.9, 50.9)	1.0 (0.8, 1.3)
40% Threshold	96.4 (86.2, 100)	70.7 (52.5, 84.4)	53.5 (28.9, 61.3)	1.9 (1.5, 2.3)
30% Threshold	100[b]	91.5 (78.6, 97.5)	67.1 (39.0, 71.2)	3.7 (3.2, 4.5)
20% Threshold	100[b]	98.8 (94.4, 100)	80.0 (56.0, 82.1)	7.6 (6.6, 8.8)

a. 95% confidence intervals constructed using 3000 bootstrap samples
b. Confidence Intervals cannot be calculated when mean sensitivity equals 100%

10 Information and Support

If there are questions regarding use of the VNS Therapy System or any of its accessories, contact LivaNova:

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Canada - https://www.canada.ca/en/health-canada.html

UK - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

EU - https://ec.europa.eu/growth/sectors/medical-devices/contacts_en