

Evoke® SCS System User Manual

Instructions for the use of the Evoke SCS System

Rx Only

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Refer to the Evoke SCS System MRI Guidelines for information on the safe use of the Evoke System in an MRI environment.

Manuals are accessible at: **https://www.saludamedical.com/manuals**.

1 Description.

This User Manual is intended for patients who have received the Saluda® Medical Evoke® SCS System for either a temporary trial or as a fully implanted system.

The Evoke SCS System is a closed-loop spinal cord stimulation (SCS) system that is intended to be used to treat chronic pain of the trunk and/or limbs. It stimulates the nerves in your spinal cord and measures their responses. It can then automatically adjust the stimulation level accordingly.

Before receiving a fully implanted system, you will go through a temporary trial period where you and your doctor can evaluate the system. If you and your doctor feel that the Evoke SCS System is right for you, you may decide to move to a fully implanted system.

The Evoke SCS System comprises several key parts to deliver your therapy:

- **Evoke External Closed-Loop Stimulator (eCLS)**. During the trial stimulation period, your leads will be connected to the Evoke eCLS. The eCLS is an external stimulator that you wear during your trial stimulation period. The eCLS delivers automatic or manually controlled therapy through your leads. The eCLS has a removable battery which is charged by a clinician or Saluda Medical representative.
- **Evoke Closed-Loop Stimulator (CLS).** The Evoke CLS is a totally implanted spinal cord stimulator that connects to your leads. The CLS is implanted under the skin for long-term therapy. The CLS delivers automatic or manually controlled therapy through your leads.
- **Evoke CAP12 Percutaneous Leads.** The Evoke CAP12 Percutaneous Leads are placed in the epidural space overlying your spinal cord. The leads are connected to the eCLS for a trial period, or permanently implanted and connected to the CLS for long-term therapy. You may have 1 or 2 leads implanted. There are 12 electrodes on each lead. This gives your clinician the ability to find the stimulation settings that best give you pain relief.
- **Evoke CAP12X Lead Extensions.** The Evoke CAP12X Lead Extensions may be used during the trial period to connect your leads to the eCLS. Your surgeon will determine if lead extensions are required.
- **Evoke Patient Controller (EPC).** The EPC allows you to control your therapy and monitor your stimulator (either a CLS or eCLS). The EPC and the stimulator communicate with each other wirelessly. The EPC kit also includes a magnet. The magnet allows you to stop stimulation from the CLS or eCLS without using the EPC.
- **Evoke Charger.** The Evoke Charger allows you to recharge the battery in your stimulator (CLS). The Charger coil (attached to the Charger) is placed on clothing covering the skin over the implanted CLS. The charge is transferred wirelessly to the CLS. The Charger is battery operated. A power adapter is included in the kit for recharging the battery in the Charger.
- **Evoke Accessory Belt.** The Evoke Accessory Belt is an elasticated belt with a pouch that you wear to hold either the eCLS or Charger coil in place.

2 Indications for use – The reasons to use the Evoke System.

The Saluda Medical Evoke SCS System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following:

- Failed back surgery syndrome
- Intractable low back pain and leg pain
- Diabetic peripheral neuropathy of the lower extremities

3 Contraindications – When the Evoke System must not be used.

The Evoke SCS System should not be used in patients who:

- Do not receive effective pain relief during trial stimulation.
- Are unable to operate the Evoke SCS System.
- Are unsuitable surgical candidates.

4 Safety information.

4.1 Warnings.

⚠**Diathermy.**

- You should not receive shortwave, microwave and/or therapeutic ultrasound diathermy.
- Diathermy generates energy that may cause heating at the lead site. This may result in tissue damage, severe injury, or death.
- It may also cause damage to the CLS. You may need surgery to replace the CLS.

⚠**Magnetic Resonance Imaging (MRI) scans.**



The Evoke System is MR Conditional depending on the version of your system, how your system is implanted and depending on how the MRI scan is performed.

- The clinical staff who will perform the MRI scan must exactly follow the instructions in the Evoke SCS System MRI Guidelines.
- There are specific recommendations for MRI scans once implanted with the Evoke System:
    - If you are undergoing a trial stimulation period with externalised leads, you should not undergo an MRI scan.

  - If an MRI scan is suggested for you, it is extremely important that you inform the clinician recommending the MRI scan that you have an implanted SCS system, along with the clinical staff who will perform the MRI scan.
  - It is also extremely important that you tell your doctor who looks after you in relation to your stimulator, if an MRI scan is suggested for you.
  - All external components of the Evoke System (e.g. Evoke Patient Controller, Evoke Charger and magnet) are MR Unsafe and must be removed before entering a room where an MRI scanner is located.
- MRI scans that are not performed according to the Evoke SCS System MRI Guidelines may:
  - Cause significant heating resulting in tissue damage, severe injury, or death.
  - Cause forces, vibrations, or torque on the device.
  - Damage the CLS and you may need surgery to replace it.
  - Cause unintended stimulation such as tingling, shocking or jolting.

Specific information for doctors and radiological staff detailing the safe conditions for MRI scanning with the Evoke System can be found in the Evoke SCS System MRI Guidelines, accessible at https://www.saludamedical.com/manuals

⚠ **CT Scans.**

- You may experience a brief increase in stimulation during a CT scan. This may cause uncomfortable stimulation, jolting or a shocking sensation.
- You should turn your stimulator off before having a CT scan.
- Consult your doctor prior to having a CT scan.

⚠ **Implanted cardiac pacemakers or defibrillators may be affected by your Evoke System.**

- You should not use your Evoke System if you have any implanted cardiac devices. They may interfere with each other.
- The effect of other implanted stimulators on your Evoke System is unknown. You should consult your doctor before having other medical devices implanted.

⚠ **Strong electromagnetic fields may cause you discomfort.**

- Avoid strong electromagnetic fields. They may cause your stimulator to switch off, cause an uncomfortable or jolting sensation, or affect communication with your EPC.
- Your stimulator may be affected by:
  - Security screeners such as those used at department stores, public buildings, and airports.
    - Show your Patient ID card and ask to go around the screener.

Note: Your stimulator may set off the security screener.

- Turn stimulation off if you have to go through the screener.

- Power cables and generators.
- Electric arc-welding devices and electric steel smelters.
- Audio speakers that contain strong magnets.
- Anti-theft devices used in shops and libraries.
- Radio communication transmitters or antennas, such as CB radio antennas. See Section 15.3.

- If you feel an effect in your stimulation from an electromagnetic field, turn off your stimulator. Move away as quickly as you can.
- Discuss with your doctor before entering any area that may affect how your stimulator works. This includes areas with a warning notice preventing entry by patients fitted with a pacemaker.

⚠ **You should not charge the stimulator while sleeping, or with the Charger or Charger coil against your skin.**

- The Charger, Charger coil and/or CLS may become hot during charging.
- If you lie on or lean against the Charger or Charger coil, it may heat up enough to cause skin redness, skin irritation or a burn.
- Ensure there are no metal objects between the Charger coil and the stimulator during charging. The metal object may heat up and cause skin redness, skin irritation or a burn. The Charger may also not work correctly.
- The Charger unit may become hot during use, with a surface temperature reaching 48 °C (118 °F). Do not hold the Charger unit for longer than 10 minutes during use. This helps to prevent skin irritation, redness or injury.
- If you feel pain or discomfort during charging, you should stop and contact your clinician.

⚠ **Before any other surgical procedures, notify your clinician or dentist that you have an implanted stimulator.**

- Some surgical procedures use electrical current that could affect your implanted stimulator and leads. This may cause serious injury to you, and/or may damage your stimulator.
- Before any procedure, tell your clinician that you have an implanted stimulator. They can then conduct the procedure without using electric current near your implanted stimulator or leads.

⚠ **If you may be allergic to parts of the stimulation system you should not be implanted with a stimulator.**

- If you are allergic to some metals or plastics, please notify your clinician. They can then check if the items you are allergic to are used in the Evoke System.

⚠ **Cables and small parts.**

- The cables in this system pose a strangulation risk. To avoid strangulation, be careful when using cables. Keep them out of the reach of children.
- Small parts and accessories could be hazardous if swallowed or cause choking if ingested or inhaled. Keep small parts and accessories out of the reach of children.

⚠ **Use in diabetic patients:**

Surgical complications and adverse events may be more frequent and severe in diabetic patients. The following additional considerations should be made for diabetic patients including:

- A pre-operative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease, those with autonomic neuropathy or renal failure, and patients with a Hemoglobin A1C (HbA1c) ≥ 8% (64mmol/mol).
- Monitor the patient's blood glucose levels in the perioperative period and instruct the patient to continue to monitor levels as they may fluctuate as a response to surgery or to complications. Implanting physicians and/or anesthesiologists should consult practice guidelines for the interoperative management of diabetic patients during surgery.
- Closely monitor the patient for signs of infection, delayed wound healing, or cerebrospinal fluid (CSF) leakage as the severity of these complications may be greater in diabetic patients.
- The physiologic closed-loop controlled (PCLC) stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.
- Frequencies greater than 1200 Hz have not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

⚠ **The Evoke System has not been tested for use in patients who are pregnant or nursing.**

⚠ **The Evoke System has not been tested for use in patients under 18 years old.**

4.2 Precautions.

Follow the instructions in this user manual.

Read and fully understand this user manual for the use of the Evoke System. Please ask your clinician if you have any questions.

⚠ **You must inform your clinician that you have an implanted stimulator before undertaking other treatments. Ask your clinician to refer to the Evoke SCS System Surgical Guide. This gives information on precautions to follow for the following treatments:**

- Ultrasound and Doppler ultrasound. These use very high frequency sound waves to create images of your internal organs or to monitor the state of a pregnancy.
- High intensity ultrasound. This uses very high frequency sound waves to create heat inside bones or muscle.
- Lithotripsy. This uses sound waves to disintegrate gallstones and kidney stones.
- Electrocautery or electrosurgery. These use an electric current to cut tissue and stop bleeding during surgery.

Implanted parts of a system should not be exposed to therapeutic levels of ultrasound energy. The implanted parts can inadvertently concentrate the ultrasound field and cause harm.

- External defibrillation. This uses a strong electric shock to the chest wall to restore rhythm to the heart.
- Radiation therapy or radiotherapy. This uses ionizing radiation, usually to control or kill malignant cancer cells.
- Ultrasound and Doppler ultrasound. These use very high frequency sound waves to create images of your internal organs or to monitor the state of a pregnancy.
- High intensity ultrasound. This uses very high frequency sound waves to create heat inside bones or muscle.
- Transcutaneous electrical nerve stimulation (TENS). This uses electric current to stimulate nerves for therapy.
- Psychotherapeutic procedures such as Transcranial Magnetic Stimulation or Electroconvulsive Therapy.
- Laser procedures.

⚠ **Operating equipment.**

The Evoke System is a SCS system that measures the patient's Evoked Compound Action Potential (ECAP) in response to stimulation. It adjusts the strength of stimulation to give stable coverage of painful areas. This is known as ECAP-controlled closed-loop stimulation.

When the stimulation is on with closed-loop stimulation enabled:

- You may leave stimulation on while operating automobiles, other vehicles, or potentially dangerous equipment.

- If you are charging the stimulator, closed-loop is disabled. So you should turn stimulation off if charging while driving or operating equipment.
- If you ever feel sudden changes in stimulation with closed-loop enabled, you should turn stimulation off before driving or operating equipment. In this case, you should contact the clinic to reprogram the closed-loop settings in the stimulator.

If the stimulation is on with closed-loop stimulation disabled:

- You may be distracted from operation of equipment if there are sudden stimulation changes.
- You should turn stimulation off before operating automobiles, other vehicles, or potentially dangerous equipment.

⚠ **Be especially careful in the six to eight weeks after your surgery.**

- In the first six to eight week after your surgery, your body will still be healing from the surgery. The implant or leads may move with some activities.
- Do not lift heavy objects greater than 11 lb. (5 kg).
- Try to limit bending, stretching or twisting as much as possible.
- Try to avoid raising your arms above your head repetitively.
- You may feel temporary pain at the implant site as the incisions heal after the surgery.
- If you notice redness or feel irritation at the wound site, contact your clinician to check for infection.

⚠ **Do not try to move your stimulator by pushing it under your skin.**

- It is normal to be able to feel the stimulator under your skin. Do not try to move it by pushing or massaging your skin.
- If you move your stimulator, it may flip over and you will not be able to charge it.
- Moving the stimulator may damage the leads or cause pain, irritation or thinning of your skin over the stimulator.

⚠ **Scuba diving.**

- You should always get advice from your clinician before scuba diving.
- You should not dive below 16 ft (5 m) or use hyperbaric chambers above 1.5 atm (150 kPa).
- Your stimulator may be damaged at greater depths or pressures.

⚠ **If you suspect part of your system is not working properly.**

If you are having problems with your system, first consult Section 13 ‘Troubleshooting’. If this does not help or you have more questions, please contact your clinician.

⚠**Do not modify or tamper.**

- Do not modify or tamper with your Evoke Patient Controller (EPC), your Charger or your external Closed-Loop Stimulator (eCLS, if you have been given one). Modifying or tampering with your equipment could cause these items not to work at all, or to work in an unpredictable way. This could lead to a loss of therapy.
- Do not connect anything to the eCLS or Charger that is not supplied as part of the Evoke System. The Charger should only be connected to the supplied power adapter. Only your clinician should connect the eCLS to lead adapters and recharge or replace the eCLS battery (refer to Section 5.5.1 'Using the eCLS'). Connecting these devices to other, unsupported items could damage them and lead to a loss of therapy.
- Do not use accessories, transducers and cables other than those specified or provided by Saluda Medical. This could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment. This could result in improper operation.

⚠**Storing your magnet when not in use.**

- Store magnet with the keeper (small metal bar) in place.
- Keep the magnet away from heat sources.
- Keep the magnet away from strong magnetic fields (e.g. other magnets).
- Handle the magnet carefully to protect it from striking hard surfaces or being dropped.

⚠**Protect the eCLS, EPC and Charger from extreme heat, cold or humidity.**

The electronics in your devices can be damaged by extreme heat, cold and humidity.

- Do not leave your devices in your car or outdoors for an extended time.
- Do not store your devices in humid environments, such as the bathroom.
- Avoid transporting or storing the eCLS at temperatures below 14 °F (-10°C) or above 131 °F (55 °C).
- Avoid transporting or storing the EPC and Charger at temperatures below -4 °F (-20 °C) or above 140 °F (60 °C).
- Allow your devices to reach room temperature for 30 minutes before use if they have been stored in cold or warm conditions.
- Only use the eCLS and EPC at temperatures of 41 °F (5 °C) to 104 °F (40 °C).
- Only use the Charger at temperatures of 41 °F (5 °C) to 86 °F (30 °C). Do not use the Charger if the temperature is above 86 °F (30 °C).

- Do not open the eCLS case. This may expose the eCLS to damaging moisture or humidity.

⚠ **Treat your eCLS, EPC and Charger gently.**

- Carry and hold your accessories carefully to protect them from striking hard surfaces or being dropped.
- Try to keep your accessories dry, and never immerse them in water.
- Do not plug the Charger into outlets that are in humid environments – such as a bathroom – or near water.
- Ensure you can always access your EPC and keep a spare set of AAA batteries at home for the EPC.
- Be sure to plug in the power adapter for the Charger somewhere easy to access.
- If you need to clean your accessories, refer to Section 10 'Maintenance of EPC, Charger and eCLS'.
- The Serial connection |O|O| on the Charger is for Saluda Medical representative use only. This connection is protected by a silicone plug. Ensure the plug is always fully inserted.

⚠ **Device malfunction or failure.**

If any of your devices, including your eCLS, EPC and, Charger, are damaged, malfunction, fail, become uncomfortably hot, emit smoke or a strange smell:

- Switch the device off immediately, stop use and contact your clinical team.
- If you use damaged or malfunctioning devices it may cause electrocution, burns, contact with hazardous chemicals, or uncomfortable stimulation.
- Please contact your clinician in the event of any device malfunction or failure.

⚠ **Battery Care.**

The EPC is powered by two disposable AAA alkaline batteries. Follow these guidelines for safe use of batteries with your EPC:

- Insert batteries the correct way by observing the plus (+) and minus (-) marks on the batteries and the EPC.
- Do not mix batteries that differ by manufacturer, brand, type, age or previous usage.
- Replace both batteries at the same time.
- Do not touch the battery contacts in the EPC.
- Do not short-circuit batteries (e.g. do not let terminals of batteries contact each other, do not place batteries loose in pockets, etc.).

- Do not disassemble, deform, immerse in water, or dispose of batteries in fire.
- Wipe batteries with a clean dry cloth if they become dirty.
- Store unused batteries in original packaging, in a clean and dry place.
- Do not use damaged or deformed batteries. If your skin or eyes contact battery fluid or liquid, wash out with water and seek medical attention immediately.
- Do not expose batteries to heat (e.g. never leave batteries in sunlight, behind a window or in a car).
- Do not recharge batteries.
- Dispose of used batteries promptly and carefully, in accordance with local regulations.
- Keep away from children.

The Charger is powered by internal rechargeable lithium ion batteries that you cannot replace.

- Only use the power adapter supplied by Saluda Medical to recharge the Charger.
- Do not touch the power adapter socket on the Charger.
- Do not leave the Charger power adapter plugged in after recharging is complete.

The eCLS is powered by a rechargeable lithium ion battery that should only be recharged or replaced by your clinician or a Saluda Medical representative.

- Do not open the case of your eCLS, remove or tamper with the eCLS battery.
- Please contact your clinic for recharge or replacement of your eCLS battery.

⚠**Disposal of your stimulator, EPC and Charger.**

- Your eCLS, EPC and Charger should be returned to your physician if you are no longer using them.
- Your eCLS, EPC and Charger contain batteries that could explode if they are thrown into a fire.

4.3 Potential risks or side effects.

All medical procedures involve some risk of injury, including death. In addition, there may be risks associated with having a SCS system that are presently unknown or unforeseeable. Despite all reasonable precautions, you might develop medical complications from having a SCS system.

Potential risks of implantation and use of a SCS system.

- Undesirable changes in stimulation sensation and/or location.
- Uncomfortable changes in stimulation (over and/or under stimulation).
- Temporary or persistent post-surgical pain at hardware implantation sites.

- CLS migration or sub-optimal placement. These may result in pain or difficulty in charging.
- Seroma or hematoma at surgery sites.
- Epidural hemorrhage, spinal cord injury, possible paralysis or other neurological complications.
- Lead migration or sub-optimal placement. These may result in undesirable stimulation changes.
- Breakage of the lead, or malfunction or failure of other system components. These may result in undesirable changes or loss of stimulation.
- Allergic response or tissue reaction to the implanted or external materials.
- Infection that may require hospitalization with intravenous antibiotic therapy.
- Infection that may result in epidural abscess that can lead to neurological harm.
- Cerebrospinal fluid (CSF) leakage with possible fistula formation.
- Gastrointestinal and/or genitourinary disruption or compromise.
- Inadequate pain relief following system implantation or over time.
- Erosion of the implanted components through the skin.
- Weakness, clumsiness, numbness, abnormal sensations or pain.
- Skin irritation.

Note: You may require surgery (including revision, explant and/or replacement) as a result of any of the above.

Note: Diabetic patients may have increased risks of infection, problems healing around the surgical site, and complications common to any surgical procedure. The severity of any surgical complication may be greater in diabetic patients, particularly those with inadequate pre-operative glycemic control.

5 Temporary trial stimulation.

To test whether you will get a benefit from the Evoke spinal cord stimulation therapy, you may have a temporary trial stimulation period.

- The trial usually lasts for up to a week, although some trials may last up to 30 days.
- During this trial stimulation period, you will have one or two CAP12 percutaneous leads implanted in your spine by your clinician in a minor surgical procedure. Your surgeon may also connect the leads to CAP12X lead extensions if required.
- After the surgery, the leads or lead extensions will be connected to an External Closed-Loop Stimulator (eCLS) to deliver stimulation pulses through your leads to your spine.
    - Your eCLS will be supplied fully charged. If the eCLS battery becomes depleted, please return to your clinic for battery recharge or replacement.
- You will control the eCLS with the Evoke Patient Controller (EPC).

5.1 Lead placement procedure.

The leads will be implanted in your back near your spinal cord:

- In this procedure, you will lie face down, awake but sedated.
- Your skin will be cleaned and anesthetized with a local anesthetic.
- The surgeon will slide a small needle in your spine.
- A lead is inserted through the needle near the spinal cord.
- The surgeon may elect to turn the stimulation on to take recordings from your spinal cord. They may test the stimulation, to make sure it is in the correct place in your back. You may feel stimulation pulses (tingling) in various areas of your body at this time.
- The surgeon may move the lead to get a better position.
- This process is repeated if you require a second lead.
- Once the leads are positioned correctly, they could be simply brought through the skin. In some cases, it may be anchored with a small anchor device under the skin and attached to a lead extension. The lead extension is then brought through the skin.
- The leads or lead extensions will be taped in place, then covered with a dressing and connected to the eCLS.
- After surgery, the eCLS will be programmed to deliver therapy according to your needs.

5.2 Programming the External Closed-Loop Stimulator (eCLS).

- Your clinician will customize a program to fit your needs.
- Your eCLS can store up to four different programs, and you can access these programs using your EPC. Refer to Section 7.

- Your eCLS may be required to be reprogrammed at any time during your trial period.

5.3 How it should feel.

- The feeling of stimulation ranges from nothing through to a tingling sensation.

⚠ **Caution:** If you feel any uncomfortable sensations, such as shocks, jolts, burning, pain or cramping around the chest or abdomen, use your EPC to adjust the level of stimulation. Refer to Section 7.

- If your therapy remains uncomfortable, contact your clinician. They can reprogram your device to restore comfortable therapy for your pain relief.
- At the end of your trial stimulation period, your clinician will ask about the amount of pain relief you experienced with the Evoke System.
    - If you and your clinician agree that your pain relief was enough (usually greater than 50% reduction in pain scores), then you will be asked to consider getting a fully implanted Evoke System.
    - If you decide to get a fully implanted Evoke System, you can expect that the sensations you feel, and the amount of pain relief will be similar to the trial period.

5.4 Lead or lead extension removal and next steps.

If you did not have lead extensions implanted:

- At the end of the trial stimulation period your leads will be removed.
- The dressings and any tape or sutures will be removed.
- The leads will then be taken out.
- This is a brief procedure, and you should not feel any pain.
- The wound will then be dressed to allow healing.
- If you decide to get an implanted Evoke System, the leads will be inserted at a similar location after your wounds from the trial have healed. See Section 6.

Note: You may notice some differences between stimulation during the trial and with the implanted stimulator. This is because the permanent leads may not be implanted in exactly the same place as the trial.

If you had a lead extension implanted and decide to get an implanted Evoke System:

- The lead extensions will be removed, but the leads will remain implanted. The leads will be connected to your implanted stimulator. See Section 6.
- If your implant surgery is scheduled for a later date after the trial period ends:

- At the end of the trial, the lead extension will be cut and remain under the skin in your back. The leads will remain implanted in the same place.
- The wound will then be dressed to allow healing.
- When you receive the fully implantable system, the remaining cut lead extensions will be removed. The leads that remained implanted after the trial will be connected to your implanted stimulator. See Section 6.

If you had a lead extension implanted and decide not to get an implanted Evoke System:

- The leads, anchors and lead extensions will be removed.
- The wound will then be closed and dressed to allow healing.

5.5 The eCLS.



Figure 5.1: The eCLS case. Your clinician will connect the eCLS to leads or lead extensions inside the eCLS case. Do not open the eCLS case.

5.5.1 Using the eCLS.

The trial leads or lead extensions are connected to lead adapters and the lead adapters are connected to the eCLS by your clinician. Your clinician will then place the eCLS inside the eCLS case (see Figure 5.1). During the trial stimulation period, you may wear the eCLS, in its case, in a pouch (see Section 9) or taped to your back. The eCLS and leads or extensions remain connected during the trial period. If the leads or extensions become disconnected from the eCLS, or you need to disconnect the eCLS for any reason, please contact your clinic.

⚠ **Caution**: Do not open the eCLS case. If your eCLS case opens please contact your clinical team (refer to Section 5.5.4.2 Reconnecting the eCLS). If you have any issues with the eCLS during your trial stimulation period, please contact your clinical team.

5.5.2 eCLS battery.

The battery in the eCLS is rechargeable and replaceable. It will be provided to you fully charged. The battery should last the duration of your trial in most cases. If your eCLS battery is depleted during your trial, you must return to your clinic to have the eCLS battery replaced or recharged.

The 'Stimulator Battery' indicator  on the EPC (see Section 7) will show a single orange bar when it is time to recharge the eCLS (see Section 7.4).

5.5.3 Stopping stimulation.

There are two ways to stop therapy:

5.5.3.1 Using the EPC.

1. Unlock the EPC by pressing  .
2. Press  to stop the therapy, or

5.5.3.2 Using a magnet.

1. Hold the provided magnet over the eCLS for 2-3 seconds until you feel stimulation stop.

Note: If you have misplaced the supplied magnet, please contact your clinician.

5.5.4 Do not open the eCLS case.

Do not open the eCLS case or remove the eCLS from the case during your trial stimulation period. Doing so could cause your leads or lead extensions to be pulled on. This may cause the leads to move and your therapy to change.

If the eCLS case is opened, the leads become disconnected from the eCLS, or you need to disconnect the eCLS for any reason, please contact your clinic.

⚠ **Caution**: Saluda Medical does not recommend that you attempt to disconnect or reconnect your eCLS without assistance.

⚠ **Caution**: Please follow the advice of your clinical team. If you wish to disconnect or reconnect your eCLS, only do so with assistance from a care-giver following the instructions below. Do not pull on the leads or extensions or apply tension between the eCLS and the leads.

5.5.4.1 Disconnecting the eCLS.

If you require the eCLS to be disconnected from the lead adapters, a care-giver should:

1. Turn stimulation off (see Section 5.5.3).
2. Open the eCLS case by separating the tabs on the eCLS case.
3. Remove the eCLS from the case.
4. Remove the lead adapters from the eCLS (see Figure 5.2), noting the port that each lead adapter was removed from.
5. Secure the lead adapters to your back using adhesive tape. This ensures they do not pull on the leads.

If the lead adapters have been removed, you should return to the clinic to have the components reconnected.

⚠ **Caution**: Do not remove the leads from the lead adapters. Do not pull on the leads or extensions or apply tension between the eCLS and the leads while the lead adapters are being disconnected from the eCLS**.**

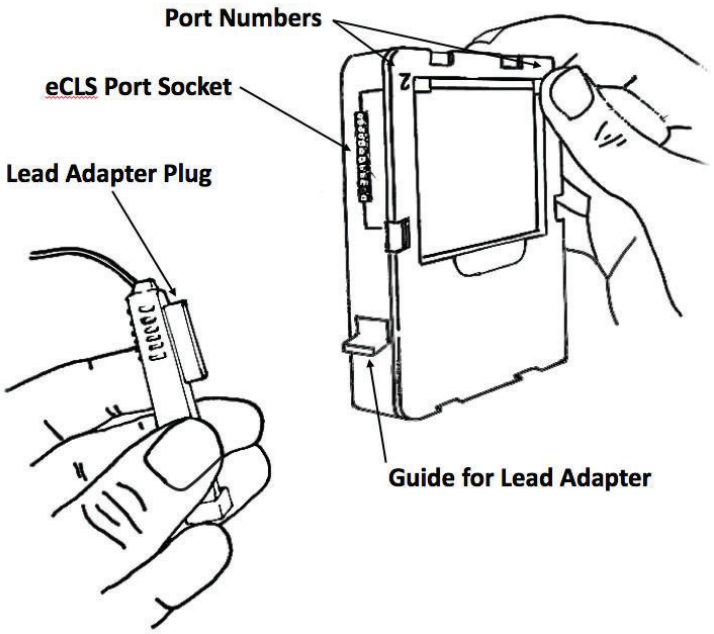


Figure 5.2: The Lead Adapter and eCLS. Port 2 of the eCLS is shown here. Port 1 is on the other side of the eCLS.

5.5.4.2 Reconnecting the eCLS

⚠ **Caution:** Saluda Medical does not recommend that you attempt to disconnect or reconnect your eCLS without assistance.

⚠ **Caution:** Please follow the advice of your clinical team. If you wish to disconnect or reconnect your eCLS, only do so with assistance from a care-giver following the instructions

below. Do not pull on the leads or extensions or apply tension between the eCLS and the leads.

If you need to reconnect the lead adapters to the eCLS, please contact the clinic.

If your clinician instructs you to have a care-giver reconnect the components, they should:

1. Rest the lead adapter on the guide on the side of the eCLS and gently push the lead adapter plug into the socket on the eCLS port until it clips into place (see Figure 5.2).

Note: The eCLS ports are labelled “1” on one side for lead 1 and “2” on the other side for lead 2.

Note: Each lead adapter must be connected to the same port it was disconnected from. If you feel stimulation has changed after reconnecting the components, your leads may have been connected to the wrong eCLS port. If your stimulation has changed or you have any issues, contact your clinic.

2. To reconnect the second lead adapter, repeat step 1.
3. Open the eCLS case and orient it as shown below (see Figure 5.3), with the orange seal side on the left and the lead exits on the top.
4. Orient the eCLS (with lead adapters connected) so that the battery is facing up and the leads are exiting from the top.
5. Place the eCLS into the left side of the eCLS case (i.e. the orange seal side of the open eCLS case; see Figure 5.3).
6. Place the leads into the slots in the seal at the lead exits.

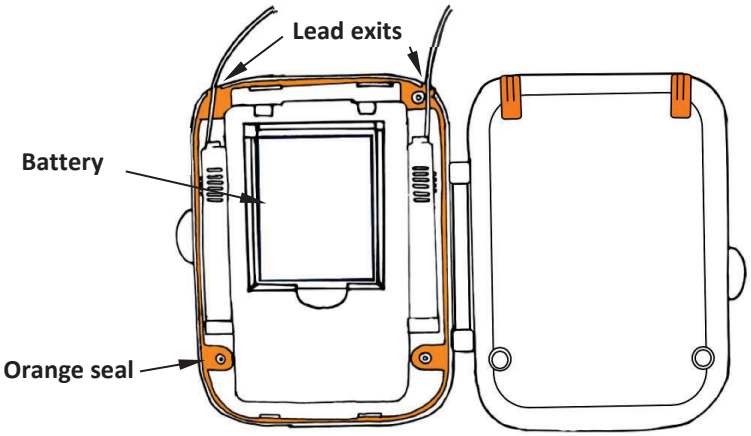


Figure 5.3: Place the eCLS with leads connected into the eCLS Case.

7. Take care to keep the leads in the slots in the seal. Close the eCLS case by folding the case shut until it snaps closed (see Figure 5.4).

⚠ **Caution:** The leads may be damaged when the case is closed if they are not in the slots in the seal at the lead exits. This could disrupt your trial stimulation.

8. Secure the eCLS comfortably to your back using adhesive tape or the Evoke Accessory Belt. See Section 9 ‘The Evoke Accessory Belt’. Avoid pulling on the leads or extensions, or applying tension between the eCLS and the leads or extensions.

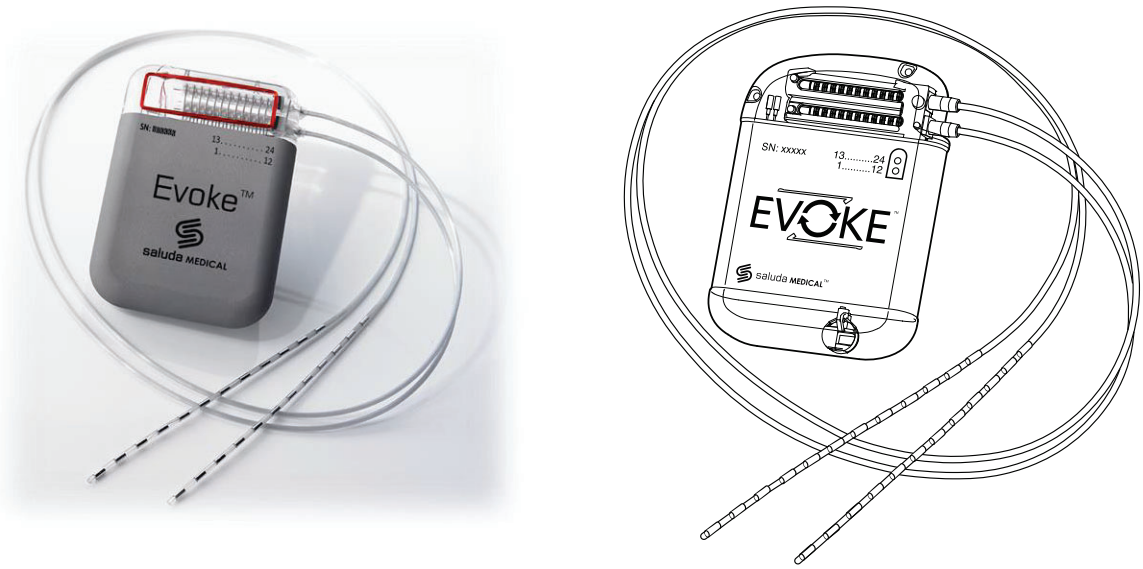


Figure 5.4 eCLS with two leads connected enclosed in the eCLS case.

6 Fully implantable Evoke System.

If you have a successful trial stimulation period, you and your doctor may decide to proceed to a fully implanted Evoke System. This includes the CLS, CAP12 leads, anchors, the EPC, and Charger. You should return your trial EPC and eCLS to your clinician.

6.1 The CLS.



REF 3002 **REF 3042**

Figure 6.1: The CLS.

The CLS is a fully implanted version of the eCLS you used in the trial.

6.1.1 Controlling the CLS.

Therapy delivered by the CLS can be controlled using your EPC. Refer to Section 7 for instructions on how to use the EPC.

6.1.2 Charging the CLS battery.

The battery in the CLS needs to be recharged regularly in order to continue delivering therapy. Refer to Section 8.2 for instructions on how to charge the CLS using the Charger.

6.1.2.1 Battery Best Practices.

You may prolong the life of your CLS battery by:

- Recharging it periodically, even if it is not fully discharged.
- Recharging it before it completely drains.
- Recharging it even if you are not using the stimulator. Recharge at least once per year.

6.1.3 Stopping stimulation from the CLS.

There are two ways to stop therapy:

6.1.3.1 Using the EPC.

1. Unlock the EPC by pressing  .
2. Press  to stop the therapy

6.1.3.2 Using a magnet.

1. Hold the provided magnet over the implant site for 2-3 seconds until you feel stimulation stop.

Note: If you have misplaced the supplied magnet, please contact your clinician.

⚠ **Caution:** Do not hold the magnet over the CLS for longer than 10 seconds or the CLS will shut down. When the CLS is shut down, the EPC will not control the CLS. To restart the CLS you must start charging (see Section 7.4). Once charging has started you will be able to control the CLS with the EPC again (see Section 7).

6.2 Lead and CLS implant procedure.

1. If your leads were removed at the end of the trial stimulation period, then new CAP12 percutaneous leads will be implanted in your spine. Your clinician will perform a surgical procedure like the temporary trial stimulation procedure described in Section 5.1.
2. The leads will be secured to prevent movement.
3. The leads are then tunneled under the skin to the CLS.
4. The leads will be connected to the CLS. The CLS will be placed 0.5 cm to 2.0 cm (0.2 in to 0.8 in) under the skin at the top of the buttocks, the flank, abdomen, or other site. The site will be chosen by you and your doctor.

Note: You should tell your doctor on which side you would like the CLS to be implanted.

5. The incisions at the lead insertion site and at the CLS site will be closed and covered with a dressing.

6.3 Programming.

- After surgery, the CLS will be configured to deliver therapy according to your needs.
- Your clinician can store up to four different programs, customized to your needs, in your implant. You can access these programs using your EPC. Refer to Section 7.
- Your implant may be re-programmed at any time if required.

6.4 How it should feel.

- The feeling of stimulation ranges from nothing through to a tingling sensation.

⚠ **Caution:** If you feel any uncomfortable sensations, such as shocks, jolts, burning, pain, or cramping around the chest or abdomen, use your EPC to adjust the level of stimulation. Refer to Section 7.

- If your therapy remains uncomfortable, contact your clinician. They can reprogram your implant to restore comfortable therapy for your pain relief.

7 The Evoke Patient Controller (EPC).



Figure 7.1: The EPC to control your stimulator (CLS or eCLS).

The EPC is for controlling your therapy. During the temporary trial stimulation period, it controls the eCLS. After you receive a permanent implant, it controls the CLS.

Your clinician will create up to four different therapy programs (refer to Section 6.3) that you can toggle between using the PROG button. Each program is customized to your needs.

7.1 EPC buttons and indicators.

EPC Lock/Unlock button.



The ‘EPC Lock/Unlock’ button turns the EPC on and off.

Turn the EPC off to lock the buttons from being able to change your therapy.

Turn the EPC on to unlock the buttons and see indicators. This enables you to stop stimulation, change programs, turn stimulation on, change therapy intensity, and check CLS and EPC battery levels.

Note: When you turn the EPC on, all of the lights will flash briefly. This is normal; you should only pay attention to the lights that remain on.

Note: The EPC will turn off and lock automatically after 2 minutes; this does not cause the stimulator to turn off.

Stop button.



Press the ‘Stop’ button to stop therapy immediately.

After turning stimulation off, you can start therapy again by pressing 

.



⚠ **Caution:** You must unlock the EPC before you can use the ‘Stop’ button.

Increase Therapy and Decrease Therapy buttons.

You can increase your therapy, from off to a comfortable level, using the ‘Increase Therapy’ button.



When you press the ‘Increase Therapy’ button to start stimulation, it will ramp up to the last level it was set to (the level indicated by the ‘Therapy intensity’ indicator light).



You can decrease your therapy using the ‘Decrease Therapy’ button.

⚠ **Caution:** You must unlock the EPC before you can use the ‘Increase Therapy’ and ‘Decrease Therapy’ buttons.



The ‘Therapy Intensity’ indicators will glow to reflect the level of your current therapy settings.

You can change the level using the ‘Increase Therapy’ and ‘Decrease Therapy’ buttons.

The number of glowing bars may not change with every click of the button, although the level of therapy will change.

When you have reached the maximum level for the current program, all seven bars will be glowing. When therapy is off, only one bar will glow. That bar indicates the level that you will start at when you press the ‘Increase Therapy’ button.

Change Program button.



Use the ‘Change Program’ button to switch between up to four different therapy programs stored in your stimulator. One of the ‘Selected Program’ indicators will glow to show the program you have selected.

1. Press the ‘Change Program’ button once and the ‘Selected Program’ indicator will start flashing.
2. Press the ‘Change Program’ button again until the desired program is selected.
3. After 2 seconds, the ‘Selected Program’ indicator will stop flashing, stimulation will turn off, and the stimulator will change to the new program.
4. Start therapy again using the 

button

⚠ **Caution:** You must unlock the EPC before you can use the ‘Change Program’ button.

Stimulator Battery Level indicator



The ‘Stimulator Battery Level’ indicator shows the battery level in the stimulator, with three green bars indicating a full charge.



⚠ **Caution:** When the orange bar appears, the battery level is low. You should recharge it right away or therapy may stop soon.

EPC Low Battery indicator.



When the 'EPC Low Battery' indicator glows orange, it indicates that the EPC battery is low. You should replace the batteries as soon as you can (see Section 7.3).

⚠ **Caution:** If you do not change the batteries, they will discharge completely. You will then not be able to use the EPC to make changes to your therapy.

Note: You can stop your therapy without the EPC by placing the provided magnet over the implanted Evoke CLS or the eCLS.

Contact Clinician indicator.



The 'Contact Clinician' indicator will glow orange if the stimulator has detected a problem. You may have you to visit your clinician for assessment.

Note: The 'Contact Clinician' indicator will not contact the clinician on your behalf. It is a message to inform you that you should contact your clinician.

7.2 EPC audio indicators.

In addition to the visual indicators on the front of the EPC, the EPC will beep to indicate various functions:

- A short beep will occur every time you press a button.
- A long beep means your EPC has successfully communicated its command to the Evoke CLS or eCLS and a change has been made.
- Two beeps indicates that the Evoke CLS or Evoke eCLS has reached a limit and did not accept the request.
    - This will occur if you are at 1 (bottom) 'Therapy Intensity' indicator light and have tried to decrease the therapy.
    - This will occur if you are at 7 (top) 'Therapy Intensity' indicator lights and have tried to increase the therapy.
    - If you think your stimulator needs to be reprogrammed, contact your clinician.
- Three beeps indicates that the Evoke CLS or Evoke eCLS did not receive the request and a change was not made.
    - Move the EPC closer to the CLS or eCLS and try again.
- Six long beeps indicate that EPC batteries are running low and should be replaced.

- Ten long beeps, followed by the EPC switching off, indicates that the CLS has gone into Safe Mode. You should contact your clinician. If you have an eCLS, it may mean that the eCLS battery needs recharging.

7.2.1 Switching audio indicators on and off.

Follow the steps below to turn off Audio indicators:

1. Turn the EPC off (if it is not already off).
2. Press and hold the  button (until you complete the next step).
3. Press and hold the  button until the EPC turns on.

Note: When the audio indicators are off you will have no indication when the stimulator has reached a limit (2 beeps), or when the stimulator did not receive the request (3 beeps). For more information, refer to Section 7.2.

Follow the steps below to turn audio indicators back on.

1. Turn the EPC off.
2. Press and hold the 

button (until you complete the next step).
3. Press and hold the  button until the EPC turns on.

7.3 Changing the battery in your EPC.

Two AAA alkaline batteries power the EPC.

To replace the batteries:

1. Slide open the back cover.
2. Remove the old batteries from the battery compartment and insert new ones. Make sure the battery terminals are placed in the orientation that is marked inside the battery compartment.
3. Replace the back cover.

7.4 Pair your EPC to your stimulator.

To enable the EPC to be used with an eCLS or CLS it must first be paired with that stimulator using the following instructions. In most cases your clinician will pair your EPC to your stimulator for you.

1. Ensure that there are no other stimulators nearby when you attempt to pair. Pairing will not occur if the EPC detects more than one stimulator.

2. With the EPC off, press and hold PROG and then press and hold at the same time for more than 1 second to enter pairing mode.
   - While searching for the stimulator, the EPC will beep every 0.5 seconds for up to 10 seconds.
   - The EPC will emit one long beep if pairing is successful.
     - The EPC will beep three times if pairing is unsuccessful because no stimulator could be detected.
     - The EPC will beep four times if pairing is unsuccessful because more than one stimulator has been detected.
3. Press to start using the EPC or to start searching again if pairing was unsuccessful.

7.5 Un-pair an EPC and stimulator.

The EPC can only be paired to one stimulator at a time. If you need to pair to a different stimulator, you must restart pairing mode as shown in Section 7.4.

Note: You do not need to un-pair the EPC from the stimulator it is already connected to before pairing with a different stimulator.

8 The Evoke Charger.



Figure 8.1: The Charger and Charger coil.

The Evoke Charger is used to charge the battery in your implanted CLS. The Charger coil is used to wirelessly transfer charge to the CLS battery.

8.1 Charger buttons and Indicators.

Start Charging button.



Place the Charger coil over the implant.

Press the ‘Start Charging’ button for more than 1 second to begin charging.

Charging Link indicator.



The ‘Charging Link’ indicator shows the quality of the link between the Charger coil and the CLS.



No charging possible.

Charger will beep every second.



Marginal alignment. Charging possible but may take longer.



Acceptable alignment for charging.

Charger will beep once if the coil alignment falls below this quality.



Ideal alignment for charging.

Note: To improve the quality of the link between the Charger coil and the Evoke CLS, move the coil closer to the implant.

Charger Battery Level indicator.



The ‘Charger Battery Level’ indicator shows the battery level in the Charger.



⚠ **Caution:** As the Charger provides the charge for recharging the CLS battery, it is important to start the charging session with a full Charger battery.

If the charge falls to one bar, recharge the Charger.

Note: Always recharge the Charger at the end of each CLS charging session to ensure you start the next charging session with a full Charger.

CLS Battery Level indicator.



The ‘CLS Battery Level’ indicator shows how much charge is left in the CLS.

Note: The ‘CLS Battery Level’ indicator should show four lit bars at the end of each charging session.



⚠ **Caution:** When the ‘CLS Battery Level’ indicator shows one bar you should recharge the CLS battery as soon as you can.

If you do not charge the CLS battery, the CLS will stop delivering therapy.

Contact Clinician indicator.



The ‘Contact Clinician’ indicator will flash six times if the Charger detects a problem with itself or the CLS.

If the ‘Contact Clinician’ indicator flashes, you need to contact your clinician so that they can investigate further.

Note: The ‘Contact Clinician’ indicator will not contact the clinician on your behalf. It is a message to inform you that you should contact your clinician during regular business hours.

8.2 Charging your Evoke CLS using the Evoke Charger.

Follow the steps below to recharge your CLS:

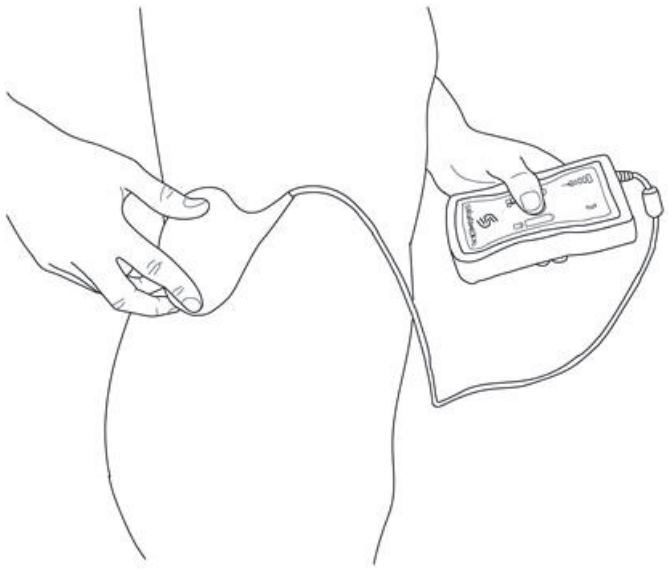


Figure 8.2: An example of positioning the Charger coil over the implant. Place Charger and Charger coil over clothing or in the Accessory Belt to ensure no extended contact with your skin.
Note: Your implant may be in a different location in your body.

1. Turn therapy off using the EPC (refer to Section 7).
2. Unplug the Charger from the power adapter.
3. Hold the Charger coil over the CLS (refer to Figure 8.2). You may place the Charger coil into the Accessory Belt pouch to hold the coil in place (see Section 9.2).
4. Place Charger and Charger coil over clothing or fabric to ensure no extended contact with your skin.
5. Press  for more than one second.
6. The Charger will beep every second until the coil starts to align with the CLS.
   - The ‘Charging Link’ indicator will then show at least two bars.
7. Move the Charger coil until the link is strongest. The ‘Charging Link’ indicator should then show three or four bars.
8. Keep the Charger coil in place over the CLS.
9. Do not wear the Charger coil on your skin for an extended time. Place clothing or the Accessory Belt between your skin and the Charger coil.
10. You may turn therapy on using the EPC once charging has started.

11. The Charger will beep once if the Charger coil moves out of charging range. Realign the Charger coil so the ‘Charging Link’ indicator shows three or four bars.
12. When charging is complete, the Charger will emit a long beep (one second). It will display four bars on the ‘CLS Battery Level’ indicator for 10 seconds.

⚠ **Caution:** Turn therapy off before you start charging. You may experience increases or decreases in therapy strength if you start charging while therapy is on. You may turn therapy on once charging has started. However, closed-loop stimulation is disabled during charging. You may experience increases or decreases in therapy strength. In some cases, the therapy may stop during charging.

⚠ **Caution:** When the orange bar on the ‘Stimulator Battery Level’ indicator on the EPC is displayed, you should charge the CLS. Your stimulator will turn off and you will not receive therapy if the battery level gets too low. If the stimulator turns off, you should charge the CLS as soon as possible.

Note: You must unlock the EPC before the ‘Stimulator Battery Level’ indicator will show.

8.3 Charger audio indicators.

In addition to its visual indicators, the Charger will beep to indicate various functions:

- A short beep will occur every time you press a button.
- A long (one second) beep indicates that the charge session is complete. All the bars glow on the ‘CLS Battery Level’ indicator for 10 seconds.
- A long (one second) beep indicates that the charge session was aborted by the user. The battery level indicator does not show.
- Three beeps indicates that the charge session has been aborted. The visual indicator show the reason why:
    - One bar glowing on the ‘Charger Battery Level’ indicator shows that Charger battery is too depleted to charge your CLS. Recharge the Charger before use (refer to Section 8.4).
    - One orange bar glowing on the ‘Charger Link’ indicator for 10 seconds indicates a poor charge link.
    - The ‘Contact Clinician’ indicator flashing on and off six times indicates a problem. You should contact your clinician to resolve the issue.

8.4 Recharging your Evoke Charger.

Follow the steps below to charge your Evoke Charger:

1. If charging, remove the Charger coil from over the CLS.
2. Plug the power adapter into a power outlet.

⚠ **Caution:** Be sure to plug the power adapter into a power outlet that is easy to access.

3. Connect the Charger to the power adapter.
4. The Charger battery level indicator will flash one to four bars every second while recharging the Charger.
5. When recharge is complete, the Charger will beep, and the 'Charger Battery Level' indicator will show four full bars (refer to Section 8.2 'Charger Battery Level indicator').

⚠ **Caution:** Do not leave the Charger power adapter plugged into a power outlet after recharging is complete.

⚠ **Caution:** You cannot recharge your Charger while you are using it to charge the CLS. You must remove the power adapter from the Charger before using it to charge your CLS.

9 The Evoke Accessory Belt.

9.1 Wearing the eCLS with the Accessory Belt.

During the trial stimulation period, you may wear an Accessory Belt to hold the eCLS. Place the eCLS into the Accessory belt using the following steps.

1. Place eCLS into the Accessory Belt pouch with the leads exiting the pouch at the top (Figure 9.1).
2. Close the pouch by pressing the Velcro sides together. The Velcro will fasten around the leads exiting the pouch.
3. Wrap the elasticated portion of the belt around your waist. Attach its Velcro end to either the pouch or the belt itself. The belt should fit comfortably and securely around your waist.
4. Position the belt so that there is no pulling or tension between the eCLS and the leads.
5. To remove the Accessory Belt, hold the pouch and lift the Velcro on the elasticated belt to separate it from the pouch or belt.

⚠ **Caution:** To avoid pulling or tension between the eCLS and the leads, the belt should not be moved during the trial (see Section 5 '

Temporary trial stimulation'). Please contact your clinician if you need to adjust the eCLS or belt.



Figure 9.1: Inserting the eCLS into the Accessory Belt.

9.2 Wearing the Charger Coil with the Accessory Belt.

The Accessory Belt can be used to hold the Charger coil in position when you are charging your CLS. Follow the steps below to use the Accessory Belt with your Charger:

1. Place the Charger coil into pouch of Accessory Belt with cable exiting the pouch at the top (Figure 9.2).
2. Close the pouch by pressing the Velcro sides together. The Velcro will fasten around the cable or leads exiting the pouch.
3. Wrap the elasticated portion of the belt around your waist. Attach its Velcro end to either the pouch or the belt itself. The belt should fit comfortably and securely around your waist.
4. Follow the Charger instructions (see Section 8.2) to charge the CLS.
5. Adjust the belt position if you need to re-align the Charge coil to the CLS.
6. When finished charging, remove the Accessory Belt. Hold the pouch and lift the Velcro on the elasticated belt to separate it from the pouch or belt.
7. The Accessory Belt is a re-usable item and may be machine washed at low temperature.



Figure 9.2: Inserting the Charger coil into the Accessory Belt.

10 Maintenance of EPC, Charger and eCLS.

You can wipe the parts periodically with a soft cloth dampened with water, alcohol or a mild detergent solution. **Do not use abrasive cleaners**.

Avoid wiping the connectors on the Charger and eCLS, if applicable.

DO NOT STERILIZE the eCLS, EPC or Charger. These items are supplied non-sterile. Sterilization could damage these devices beyond repair. You may be unable to use your stimulation system.

Contact your clinician for troubleshooting or possible replacement if your device is not function as expected.

11 Disposal of devices.

⚠ **Caution:** Your eCLS, EPC and Charger contain batteries that could explode if they are placed into a fire.

The eCLS, EPC and Charger must not be discarded in the normal municipal waste. Please return to Saluda Medical for disposal via your clinical team.

12 Patient ID Card.

Every CLS is supplied with a Patient ID card for the clinician to complete and give to you.

Keep this card some place safe, as you may need it to show to doctors or nurses who you see for other reasons. This is so they understand you have an SCS system implanted. You may also need to show security personnel in shops or airports if the implant triggers detectors.

Importantly, your Patient ID Card will tell medical staff that you can have a MRI Scan only under very specific conditions. If an MRI scan is suggested for you, you must inform the MRI clinical staff that you have an implanted SCS system that is considered MR Conditional. You should also inform your pain management physician of any MRI procedures being considered. Refer the MRI clinical staff to the Evoke SCS System MRI Guidelines.

13 Troubleshooting.

If you are experiencing problems with your system refer to the suggestions below and contact your clinical team.

Table 13.1: Troubleshooting.

Issue	Resolution
 The 'Contact Clinician' indicator on my EPC or Charger is glowing.	The stimulator has detected a problem that requires you to visit your Clinician for assessment. **Please contact your clinical team at your first opportunity and remember to take your EPC and Charger with you**. **Note:** You will not be able to charge the stimulator if the 'Contact Clinician' indicator is flashing on your Charger.
During charging, my Charger beeps continuously.	The Charger will beep once per second when there is a poor link between the Charger and the CLS. Reposition the Charger coil over the implant so that the 'Charging Link' indicator shows at least 2 bars  . **Note:** Wait about 1 second between each reposition in order for the Charger to update the link.
My Charger started beeping during charging.	The link between the Charger coil and your CLS has dropped below two bars so charging is no longer possible. Adjust the position of the coil until the 'Charging Link' indicator displays at least two bars as shown above.

Issue	Resolution
Charger will not turn on, or (during charging) beeped 3 times and turned off.	Press and hold the 'Start Charging' button for 2 seconds. If nothing happens, or the Charger battery indicator is below 1 bar, plug the Charger into the power adapter. Refer to Section 8.4. Once the Charger battery indicator is full, disconnect from the power adapter and try to charge again. Refer to Section 8. 
My EPC stimulation level indicator lights do not change when I increase or decrease stimulation.	Sometimes you will need to press the START or button multiple times before the lights will change. This is normal. However, you should feel a change in stimulation intensity almost every button press. If you feel you need to be reprogrammed, please contact your clinical team.
My therapy has stopped.	The stimulator will stop stimulation if it detects an issue or if the stimulator battery is too low. First try to restart your stimulator with your EPC. If the EPC does not connect to the stimulator, then refer to 'Stimulator Battery too low' below. If the EPC connects, but stimulation does not start, or it stops stimulation repeatedly, try the suggestions below. **If you have an eCLS** 1. Stimulator battery too low: a. Please contact your clinical team to organize battery recharge or replacement. 2. Lead Disconnection: a. Do not open the eCLS Case. b. Please contact your clinical team. **If you have a fully implanted CLS** 1. Stimulator Battery too Low: a. Place the Charger coil over the CLS and press the 'Start Charging' button for 2 seconds. b. If the CLS battery was low, then recharge it. Refer to Section 8. Then restart stimulation. Refer to Section 7.

Issue	Resolution
Stimulation strength becomes more variable.	This may happen during charging. It should resolve once charging is finished. If this happens often when not charging, you should contact your Clinician to reprogram your stimulator.
Stimulation strength suddenly decreases.	When the stimulation reaches some internal limits, it may decrease in strength automatically. You will be able to increase the strength again with your EPC. If this problem continues you may need to contact your Clinician to reprogram your stimulator.
The EPC will not turn on.	The batteries that power the EPC may have run low. Refer to Section 7.3 for instructions on how to replace the batteries in the EPC.
My EPC does not appear to be working.	**If the stimulation is still on** For help on performing any steps, refer to Section 7. **Ensure that the EPC is on when performing the steps below.** 1. Low battery: a. If the 'EPC low battery indicator' light is on you should change the batteries. 2. EPC not communicating with the stimulator: a. Turn on the audio indicators (if they are off). b. Try to use the EPC again, if you hear 2 or 3 beeps this means the command is not getting through to the stimulator. c. Bring the EPC closer to the stimulator and try again. If you have a CLS, bring the EPC to the side where the CLS is implanted, or try to hold it directly behind the implant site. **If the stimulation is off** 1. See 'My therapy has stopped'.
I cannot change programs.	To change programs, you will have to press the PROG  button once (**do not hold it**). **Then press it again while it is still flashing** until you select your desired program. Refer to Section 7. If your program light does not change from Program 1 then you have only been given one program. Contact your clinical team if you think your stimulator needs to be reprogrammed.

Issue	Resolution
Stimulation does not get stronger when you press the  button .	When the stimulation reaches some internal limits, it will not increase. It may not show as 7 bars on the EPC. It may be fixed by changing posture or changing programs. If this continues you may need to contact your Clinician to reprogram your stimulator.

14 Package contents.

Table 14.1: Package Contents.

Evoke Patient Controller (EPC) **(Ref No: 3040)**	1 x Evoke Patient Controller (EPC) 2 x AAA Batteries 1 x Magnet
Evoke Charger **(Ref No: 3006)**	1 x Evoke Charger 1 x Evoke Power Adapter
Evoke Accessory Belt **(Ref No: 3039)**	1 x Evoke Accessory Belt

15 Technical Specifications.

Note: All measurements in Technical Specifications are approximate

15.1 Device Specifications.

15.1.1 Evoke CLS (REF 3002)

Table 15.1: Evoke CLS Specification for REF 3002

Materials	Case	Titanium
	Header	Epoxy
	Seals	Liquid silicone rubber
	Connector springs	Platinum Iridium (24 x connectors)
	Set screw	Stainless steel
Dimensions	68 mm x 48 mm x 12 mm (2.7 in x 1.9 in x 0.472 in)	
Volume	33 cm^3 (2 in^3)	
Weight	50 g (1.76 oz.)	
Lead ports	2	Each lead is secured by a set screw at the port entry
Electrodes	25 CLS case is electrode 25 (recording only)	Port 1: electrodes 1-12 Port 2: electrodes 13-24
Stimulation parameters	Current	0 mA – 50 mA (20 mA @750 Ω)
	Pulse Width	20 µs – 1000 µs
	Frequency	10 Hz – 1400 Hz

Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3002
*Channels are automatically selected when the communication session begins.		
Battery	Battery type	200 mAh Li-Ion rechargeable battery
	Battery life	Greater than 10 years at moderate settings (current = 5.0 mA, pulse width = 200 µs, frequency = 60 Hz, impedance = 750 Ω, 24hrs/day usage)*
*End of Battery Life is defined by Saluda Medical as the point at which the device can no longer maintain enough charge to provide 24 hours of therapy. At higher or lower settings, this defined end of life could be shorter or longer respectively.		
Charging	Transcutaneous charging using inductive coupling with an external coil	
	Implant depth	5 mm to 20 mm (0.2 in to 0.8 in)
Recording amplifier gain	Low: 250x High: 1000x	
Data recording	32 MB, up to 1 year (Stimulation usage, ECAP amplitude and current statistics)	
Radio opaque identifier	"SME BYY" Where "SME" is Saluda Medical, "B" is the CLS model and YY is the two-digit year of manufacture	
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F) Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm) Max: 150 kPa (1.48 atm)

15.1.2 Evoke CLS (REF 3042)

Table 15.2 Evoke CLS Specification for REF 3042

Materials	Case	Titanium
	Header	Epoxy
	Seals	Liquid silicone rubber
	Connector springs	Platinum Iridium (24 x connectors)
	Set screw	Stainless steel
Dimensions	67.5 mm x 47.7 mm x 11 mm (2.65 in x 1.88 in x 0.43 in)	
Volume	32.6 cm^3 (2.3 in^3)	
Weight	49 g (1.73 oz.)	
Lead ports	2	Each lead is secured by a set screw at the port entry
Electrodes	25 CLS case is electrode 25 (recording only)	Port 1: electrodes 1-12 Port 2: electrodes 13-24
Stimulation parameters	Current	0 mA – 50 mA (20 mA @750 Ω)
	Pulse Width	20 µs – 1000 µs
	Frequency	10 Hz – 1400 Hz
Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3042
*Channels are automatically selected when the communication session begins.		
Battery	200 mAh Li-Ion rechargeable	
Battery life	Greater than 10 years* at moderate settings. (current = 5.0 mA, pulse width = 200 µs, frequency = 60 Hz, impedance = 750 Ω, 24hrs/day usage). Greater than 10 years* for more than 95% of patients.	

*End of CLS Battery Life is defined by Saluda Medical as the point at which the device can no longer maintain enough charge to provide 24 hours of therapy. At higher or lower settings, this defined end of life could be shorter or longer respectively.

Charging	Transcutaneous charging using inductive coupling with an external coil Implant depth	5 mm to 20 mm (0.2 in to 0.8 in)	
Recording amplifier gain	Low: 250x High: 1000x		
Data recording	32 MB, up to 1 year (Stimulation usage, ECAP amplitude and current statistics)		
Radio opaque identifier	"SME EYY" Where "SME" is Saluda Medical, "E" is the CLS model and YY is the two-digit year of manufacture		
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)

15.1.3 Evoke eCLS (includes Case and Lead Adapters).

Table 15.3: Evoke eCLS Specification.

Materials	eCLS body and case	ABS Plastic
	Case seal	TPE
Dimensions	100 mm x 85 mm x 20 mm (3.9 in x 3.4 in x 0.8 in)	
Weight	96 g (3.4 oz.)	
Electrodes	24	Port 1: electrodes 1-12, Port 2: electrodes 13-24
Functional specifications	All other functional specifications are the same as the CLS (See Section 15.1.1)	
Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3036
*Channels are automatically selected when the communication session begins.		
Battery	800 mAh Li-ion rechargeable	
Battery Life	Greater than 14 days between charges at moderate settings. Greater than 7 days between charges for more than 95% of patients.	
Charging	Li-Ion battery charger	
Ingress Protection **eCLS in case**	IP22 Rating for protection against access of solid objects greater than or equal to 12.5 mm, and for vertically dripping water when the device is tilted 15 degrees.	
eCLS	IP30 Rating for protection against solid objects greater than or equal to 2.5mm, and no protection against water.	
IEC 60601-1 / **EN 60601-1 Classification**	Type BF Applied Part Internally Powered Medical Electrical Equipment Continuous Operation	

Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
	Humidity:	Min: 0% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106kPa (1.05 atm)
Operating Conditions	Temperature:	Min: 5 °C (41 °F)	Max: 40 °C (104 °F)
	Humidity:	Min: 15% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106 kPa (1.05 atm)

15.1.4 Evoke Lead Adapters.

Table 15.4: Evoke Lead Adapters Specification

Materials	Body	ABS Plastic
Dimensions	55 x 13 x 13 mm (2.2 x 0.5 x 0.5 in)	
Lead connection	Ports	1
	12 spring connectors	Au plating on stainless steel
Lead Adapter to eCLS connection	12 pin plug	

15.1.5 Evoke CAP12 Percutaneous Lead (includes Trial Leads).

Table 15.5: Evoke CAP12 Percutaneous Lead Specification

Materials	Lead body	Pellethane	
	Lead ends	Pellethane	
	Distal electrodes	Platinum Iridium	
	Proximal connectors	Platinum Iridium	
	Retention ring	MP35N[1]	
	Conductors	35N LT with Ag core (19 strand cable)	
Dimensions	Lengths	60 cm (1.97 ft.) or 90 cm (2.95 ft.)	
	Diameter	1.32 mm (0.05 in)	
Electrodes	Number	12	
	Length	3 mm (0.12 in)	
	Pitch	7 mm (0.276 in)	
Connectors	Length	1.02 mm (0.040 in)	
	Pitch	1.96 mm (0.077 in) center to center	
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)
	[1] Alloy of Nickel, Cobalt, Chromium and Molybdenum. MP35N is not in contact with tissue but may be in contact with body fluid.		

15.1.6 Evoke CAP12X Lead Extension.

Table 15.6: Evoke CAP12X Lead Extension Specification

Materials	Lead extension body	Pellethane	
	Lead extension ends	Pellethane	
	Proximal connectors	Platinum Iridium	
	Retention ring	MP35N[1]	
	Connector springs	Platinum Iridium	
	Set screw	Titanium	
	Header body	Silicone	
Dimensions	Length	55 cm (1.8 ft.)	
	Body Diameter	1.32 mm (0.05 in)	
	Header Length	41 mm (1.62 in)	
	Header Diameter	5.45 mm (0.21 in)	
Connectors	Number	12	
	Length	1.02 mm (0.040 in)	
	Pitch	1.96 mm (0.077 in) center to center	
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)
	[1] Alloy of Nickel, Cobalt, Chromium and Molybdenum. MP35N is not in contact with tissue but may be in contact with body fluid.		

15.1.7 Evoke Anchors.

Transport and store anchors at temperatures from -10 °C (14 °F) to 55 °C (131 °F). Operate surgical accessories at pressures from 70kPa (0.69 atm) to 106kPa (1.05kPa).

Table 15.7: Evoke Anchors Specification

Suture Anchor	**Form**	Two suture eyelets	
	Material	Silicone rubber	
	Diameter	5 mm (0.20 in)	
	Length	34 mm (1.34 in)	
Active Anchor	**Form**	Three suture eyelets, and a set screw to secure the lead	
	Materials	Body	Silicone rubber
		Set screw	Titanium
		Set Screw Block	Titanium
	Height	6.7 mm (0.26 in)	
	Length	34.2 mm (1.35 in)	

15.1.8 Evoke EPC.

Table 15.8: Evoke EPC Specification

Materials	Body and Battery Cover	ABS Plastic	
	Buttons and Seal	TPE	
	Lens	Polycarbonate	
Dimensions	90.4 mm x 49.9 mm x 24.5 mm (3.55 in x 1.96 in x 0.96 in)		
Weight	73 g (2.56 oz)		
Radio frequency communication	MICS band	402 - 405 MHz	
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55	
	Transmit/Receive Channel Bandwidth	300 kHz	
	Modulation type	Frequency Shift Keying (FSK)	
	Range	1.0 m (3.3 ft.)	
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum	
	FCC ID	2AYGR-3040	
*Channels are automatically selected when the communication session begins.			
Battery	2 x AAA Alkaline batteries. Approx. 2000mAh.		
Battery Life	Greater than 60 days (dependent on usage)		
Expected Service Life	Greater than 1 year		
Ingress Protection	IP22 Rating for protection against access of solid objects greater than or equal to 12.5 mm, and for vertically dripping water when the device is tilted 15 degrees.		
IEC 60601-1 / EN 60601-1 Classification	Type BF Applied Part Internally Powered Medical Electrical Equipment Continuous Operation		
Storage & Transportation Conditions	Temperature:	Min: -20 °C (-4 °F)	Max: 60 °C (140 °F)
	Humidity:	Min: 0% RH	Max: 90% RH
	Pressure:	70kPa (0.69 atm)	Max: 106 kPa (1.05 atm)
Operating Conditions	Temperature:	Min: 5 °C (41 °F)	Max: 40 °C (104 °F)
	Humidity:	Min: 15% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106 kPa (1.05 atm)

15.1.9 Evoke Charger.

Table 15.9: Evoke Charger Specification

Materials	Charger	ABS Plastic	
	Control panel	PET	
	Charger coil	Silicone	
Dimensions	Charger	139.7 mm x 82.6 mm x 26.2 mm (5.50 in x 3.25 in x 1.03 in)	
	Charge coil	Cable length	60 cm (2 ft)
		Diameter	10 cm (3.9 in)
		Thickness	7 mm (0.28 in)
Weight	410 g (14.48 oz)		
Communication Link	Inductive coupling		
Battery	2 x 18650 Lithium ion protected cells. 5200 mAh		
Charging	Via the supplied power adapter		
Battery Life	Greater than 5 years* at moderate settings Greater than 3 years* for at least 95% of patients * End of Charger battery life is 300 full charge and discharge cycles of the Charger battery.		
Expected Service Life	Greater than 1 year		
Ingress Protection	IP22 Rating for protection against access of solid objects greater than or equal to 12.5 mm, and for vertically dripping water when the device is tilted 15 degrees.		
IEC 60601-1 / EN 60601-1 Classification	Type BF Applied Part Internally Powered Medical Electrical Equipment Continuous Operation		
Storage & Transportation Conditions	Temperature:	Min: -20 °C (-4 °F)	Max: 60 °C (140 °F)
	Humidity:	Min: 0% RH	Max: 90% RH
	Pressure:	70kPa (0.69 atm)	Max: 106 kPa (1.05 atm)
Operating Conditions	Temperature:	Min: 5 °C (41 °F)	Max: 30 °C (86 °F)
	Humidity:	Min: 15% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106 kPa (1.05 atm)
Supplied Power Adapter Rating	Input Voltage	100-240 Vac, Class II Medical Electrical Equipment	
	Input Current	Max 0.3 A	

Note: Power adapter isolates the Charger from the mains power	Frequency	50 - 60 Hz
	Output Voltage	8.4 Vdc
	Output Current	Max 1.3 A
	Ingress Protection	IP22 Rating

15.1.10Evoke Accessory Belt.

Table 15.10: Evoke Accessory Belt Specification

Materials	Belt	Elasticized poly/cotton
	Belt fastener	Hook and loop fastener
	Pouch front	Brushed poly/cotton
	Pouch back	Perforated nylon
	Pouch fastener	Hook and loop fastener
Dimensions	Belt	85 mm x 960 mm (3.3 in x 37.8 in) unstretched
	Pouch	140 mm x 270 mm (5.5 in x 10.6 in) unstretched
Storage Temperature Limitations	Low: -10 °C (14 °F)	High: 55 °C (131 °F)

15.2 Wireless Communication.

15.2.1 Quality of Service & Wireless Coexistence.

The Evoke SCS System employs a wireless communication link operating in the 402-405 MHz MICS frequency band. This band is designated for implantable medical devices and enables communication between the CLS/eCLS and the EPC.

At the beginning of each communication session, the EPC automatically scans 8 channels in the frequency band and selects the least congested channel for communication. All communication is error checked and is retried automatically. The user is notified if the wireless communication link fails to connect.

The communication range between the EPC and the CLS/eCLS is typically 1 m (3.3 feet). If you experience issues with the wireless communication between the EPC and CLS/eCLS, try the following:

- Hold the EPC closer to the CLS/eCLS.
- Move away from other devices that may be causing interference (see Section 15.3).
- Wait a few minutes and try connecting again.
- Do not operate other wireless devices, such as a mobile phone, tablet or laptop, at the same time.

15.2.2 Wireless Security.

The Evoke SCS System has a communication range of 1 m (3.3 feet). To enable the EPC to communicate with an eCLS or CLS, it must first be paired with that stimulator. The EPC may communicate with only one CLS or eCLS at a time. The stimulator will not respond to any communication that does not come from a paired device. Additional mechanisms are in place to safeguard the integrity of the communication. There are no security settings that require input or control by the user.

15.3 Electromagnetic Interference.

The following tables indicate the electromagnetic environment in which the Evoke SCS System is intended to operate. This is to ensure compliance with international standards for the electromagnetic interference (EMI) produced by the Evoke SCS System or the susceptibility of the Evoke SCS System to EMI. For more information on this section please contact a Saluda Representative.

⚠**Caution:** Use of accessories, transducers, and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

15.3.1 Guidance and Manufacturer's Declarations.

Table 15.11 Electromagnetic emissions.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.		
Emissions Test	**Compliance**	**Electromagnetic environment – guidance**
Radiated disturbance, 30 MHz -6000 MHz CISPR 11 (EN 55011)	Group 1, Class B	The Evoke SCS System is unlikely to produce electromagnetic interference with nearby electronic equipment.
Conducted Emissions 0.15 MHz - 30 MHz CISPR 11 (EN 55011)	Class B	The Evoke SCS System is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable for the battery powered devices or device consuming less than 75 W from mains power outlet (Charger with power adapter)	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Not applicable for the battery powered devices. Charger with power adapter complies with requirements of the standard	

Table 15.12 Electromagnetic immunity - electrostatic discharge and mains power.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.			
Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic environment – guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV air	±2 kV, ±4 kV, ±6 kV, ±8 kV contact ±2 kV, ±4 kV, ±8 kV, ±15 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%
Electrical fast transient/burst IEC 61000-4-4	± 2 kV gaseous discharge at 100 kHz repetition frequency	± 2 kV @100 kHz repetition frequency for power supply lines to Charger power adapter.	Mains power quality should be that of a typical household, commercial or hospital environment. If the user of the Charger power adapter requires continued operation during mains power interruptions, it is recommended that the Charger power adapter be powered from an uninterruptible power supply or a battery.
Surge Immunity IEC 61000-4-5	± 0.5 kV, ± 1 kV	± 0.5 kV, ± 1 kV power supply line to Charger power adapter.	
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0 % residual voltage; 1 cycle, and 70% residual voltage; 25/30 cycles Single phase: at 0 ° Voltage Interruptions: 0% residual voltage; 250/300 cycles	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0% residual voltage for 1 cycle at 0 °; 70% residual voltage for 25 cycles at 0 °; Voltage Interruptions: 0% residual voltage for 250 cycles at 0 °; Interval between Events – min. 10s; Test cycle – 3 times;	
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m 50/60 Hz	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical household, commercial or hospital environment.

Table 15.13 Electromagnetic immunity – radio frequency.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.

⚠**Caution:** Portable and mobile RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer to any part of the Evoke SCS System, including cables, than the recommended separation distance stated below (0.3 m, 12 inches). Otherwise, degradation of the performance of this equipment could result.

⚠**Caution:** Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic environment – guidance**
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz; 6 Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz 80 % AM at 1 kHz	The Charger power adaptor functioned correctly during the test. Not applicable for the battery-powered devices.	The separation distance between an interfering RF transmitter and any Evoke SCS should be greater than 0.3 m and the maximum power from the RF transmitter should not exceed 2W or 28 V/m at a distance of 0.3 m.
Radiated RF IEC 61000-4-3	10 V/m 80 MHz to 2.7 GHz 80% AM at 1 kHz	3 V/m for professional healthcare facility environment or 10 V/m for home healthcare environment	
Proximity fields from RF wireless communications equipment	Up to 28 V/m at 0.3m at specified frequencies (refer Table 9, IEC 60601-1-2)	Tested at up to 28 V/m, devices continued to function during test.	

15.4 Federal Communications Commission (FCC).

15.4.1 Interference Statement for CLS, eCLS, EPC

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
- Consult the dealer or an experienced radio/TV technician for help.

⚠**FCC Caution:** Any changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate this equipment.

This transmitter must not be co-located or operating in conjunction with any other antenna or transmitter.

The devices in the Evoke System may not interfere with stations operating in the 400.150 – 406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

For MedRadio transmitters operating in the 401-406 MHz band, the following statement applies:

> This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter

has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

15.4.2 Charger

This device complies with Part 18 of the FCC Rules.

15.4.3 Radiation Exposure Statement.

The products comply with the FCC portable RF exposure limit set forth for an uncontrolled environment and are safe for intended operation as described in this manual.

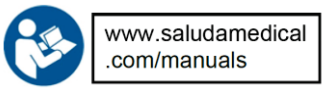
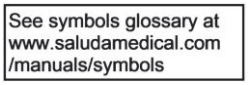
16 Glossary.

Table 16.1: Glossary.

Term	Definition
Accessory Belt	An elastic belt with a pouch to hold an eCLS or a Charger coil.
Charger	The device that charges the battery in the CLS.
Charger coil	A circular paddle connected to the Charger that is held over the CLS to charge the CLS battery.
Charger Power Adapter	The power supply adapter for the CLS/eCLS Charger.
Closed-Loop (CL) Stimulation	Stimulation that is automatically adjusted in response to measurements from the spinal cord nerves (ECAP) to maintain stable therapy. This is also known as ECAP-controlled closed-loop stimulation.
Closed-Loop Stimulator (CLS)	An implantable pulse generator capable of ECAP-controlled closed-loop stimulation.
Electrode	An electrical contact used to deliver stimulation current or to measure responses from spinal cord nerves.
Evoke Patient Controller (EPC)	A remote control that allows the patient to adjust the therapy output from the CLS/eCLS.
Evoked Compound Action Potential (ECAP)	The electrical signal from multiple nerve fibers in response to an electrical stimulus pulse.
External Closed-Loop Stimulator (eCLS)	The eCLS is a non-implantable device with the same functionalities as the CLS.
Lead	Insulated cable with exposed electrodes at the distal end used in neurostimulation therapy.
Lead Adapter	An adapter to connect leads or lead extensions to the eCLS during the trial stimulation period.
Lead Extension	Insulated cable that is connected to a lead for temporary use during the trial stimulation period.
Spinal Cord Stimulation (SCS)	A treatment for chronic pain using pulsed electrical signals delivered to the spinal cord.
Stimulation	The application of electrical current through electrodes.

17 Symbols.

Table 17.1: Symbols.

Symbol	Definition
	Follow the instructions for use on this website: www.saludamedical.com/manuals
	Follow the instructions for use
	Follow the instructions for use at this website: www.saludamedical.com/manuals
	Symbols Glossary can be found on this website: www.saludamedical.com/manuals/symbols
	Catalogue number
	Serial number
	Lot number
 YYYY-MM-DD	Use by date (YYYY = year, MM = month, DD = day)
	Caution
	Temperature limitation (°F and °C)
	Manufacturer
 YYYY-MM-DD	Date of manufacture (YYYY = year, MM = month, DD = day)
	Do not dispose of this product in the unsorted municipal waste stream – dispose of this product according to local regulations
	Type BF applied part
	Non-ionizing electromagnetic radiation
	Do not use if package is damaged

Symbol	Definition
	MR Conditional: Refer to Evoke SCS System MRI Guidelines at https://www.saludamedical.com/manuals
	Magnetic Resonance (MR) unsafe: External components of the Evoke SCS System are MR Unsafe.
IP22	Ingress Protection Rating 22: • Protected against access of solid foreign objects greater than or equal to 12.5mm diameter. • Protected against vertically dripping water when the device is tilted 15 degrees.
IP30	Ingress Protection Rating 30: • Protected against solid objects greater than or equal to 2.5mm, and no protection against water.
	Class II Medical Electrical Equipment
	Power supply connection
	Serial Connection
Rx Only	Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner
	Federal Communications Commission (FCC) symbol indicates that the device is FCC compliant

18 Contact us.

Most questions you have about your Evoke SCS System can be answered by reading this manual or looking at our website, www.saludamedical.com and/or www.saludamedical.com/manuals.

If you have any further questions, please email us at info@saludamedical.com.

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Evoke® SCS System Clinical Summary

Clinical study evidence supporting the use of the Evoke™ SCS System

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Refer to the Evoke SCS System Surgical Guide for:

- System warnings and precautions

Manuals are accessible at https://www.saludamedical.com/manuals.

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I. DESCRIPTION

The Saluda® Medical Evoke® SCS System is a Spinal Cord Stimulation (SCS) system that incorporates ECAP-controlled closed-loop stimulation for the management of chronic, intractable pain. The Evoke System measures evoked compound action potentials (ECAPs) and may be programmed to deliver either ECAP-controlled closed-loop SCS or fixed-output open-loop SCS.

This Clinical Summary presents the clinical study evidence supporting premarket approval (PMA) of the Evoke SCS System.

II. ORIGINAL INDICATION

The original PMA (P190002) for the Evoke Spinal Cord Stimulation (SCS) System ("Evoke System") was approved for the indication as an aid in the management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with any of the following: failed back surgery syndrome, intractable low back pain and leg pain.

The summary of primary clinical studies supporting the original PMA of the Evoke System is summarized in section II.A below.

II.A. Summary of Primary Clinical Studies

Approval was supported by a pivotal clinical study designed to evaluate the safety and effectiveness of the Evoke System for treatment of chronic, intractable pain of the trunk and/or limbs in the US under an IDE (Evoke study). Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

Additionally, long-term safety and effectiveness of the Evoke System is supported by a clinical study performed in Australia (Avalon study) and is summarized in section II.B.1.

1. Study Design

The Evoke pivotal clinical study was a prospective, multicenter, randomized, double-blind, clinical trial. The study was designed to compare the use of ECAP-controlled, closed-loop stimulation to open-loop stimulation. The Evoke System open-loop stimulation mode is equivalent to other commercially available SCS systems. Because the Evoke System additionally features the ability to measure ECAPs in both open- and closed-loop stimulation modes, use of the Evoke System in both treatment groups allowed for a more direct comparison of spinal cord activation between groups. Thus, the study population was randomized to either the Evoke System closed-loop stimulation mode (Investigational group) or to open-loop stimulation (representative of treatment with commercially available SCS systems) using the Evoke System open-loop stimulation mode (Control group). Spinal cord activation was measured via ECAPs in both treatment groups.

Subjects, Investigators, and investigational site staff were blinded to the treatment assignment (double-blind). Subjects were randomized in a 1:1 ratio to the treatment arms and a frequentist statistical analysis was performed. The primary objective of the study was to demonstrate that outcomes related to chronic intractable trunk and/or limb pain were at least as good (non-inferior) when using closed-loop SCS compared to open-loop SCS. Additionally, if non-inferiority was established, the study was designed to further assess the potential superiority of closed-loop SCS for treatment of chronic intractable trunk and/or limb pain compared to open-loop SCS. The required sample size was 120 subjects total (60 subjects in each treatment group). To account for potential drop-out, a total of up to 134 subjects (67 subjects in each treatment group) could be randomized.

An independent, blinded Clinical Events Committee (CEC) reviewed and adjudicated all adverse events occurring in the study. An independent, blinded Medical Monitor provided guidance on the study.

Clinical Inclusion and Exclusion Criteria

Enrollment in the Evoke study was limited to patients who met the following inclusion criteria:

a. Subject is male or female between the ages of 18 and 80 years.
b. Have been diagnosed with chronic, intractable pain of the trunk and/or limbs, which has been refractory to conservative therapy for a minimum of 6 months.
c. VAS leg pain score ≥ 6 cm.
d. VAS back pain score ≥ 6 cm.
e. VAS overall trunk and limb pain score ≥ 6 cm.
f. Be an appropriate candidate for an SCS trial and the surgical procedures required in this study based on the clinical judgment of the Investigator.
g. Prescribed pain medications have been stable for at least 30 days prior to the baseline evaluation.
h. ODI score of 41-80 (severely disabled or crippled) out of 100 at the baseline evaluation.
i. Be willing and capable of giving informed consent and able to comply with study-related requirements, procedures, and visits.
j. The subject's primary back pain is located such that lead placement will be in the thoracolumbar region.

Patients were not permitted to enroll in the Evoke study if they met any of the following exclusion criteria:

a. Have a medical condition or pain in other area(s), not intended to be treated with SCS, that could interfere with study procedures, accurate pain reporting, and/or confound evaluation of study endpoints, as determined by the Investigator.
b. Have evidence of an active disruptive psychological or psychiatric disorder or other known condition significant enough to impact perception of pain, compliance of intervention, and/or ability to evaluate treatment outcomes.
c. Are not a surgical candidate due to a diagnosis of an uncontrolled coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, uncontrolled diabetes mellitus, or morbid obesity.
d. Have an existing drug pump and/or SCS system or another active implantable device such as a pacemaker, deep brain stimulator (DBS), or sacral nerve stimulator (SNS).
e. Have prior experience with SCS.
f. Have a condition currently requiring or likely to require the use of MRI or diathermy.
g. Have a life expectancy of less than 1 year.
h. Have an active systemic infection or local infection in the area of the surgical site.
i. Be allergic, or have shown hypersensitivity, to any materials of the neurostimulation system which come in contact with the body.
j. Be pregnant or nursing (if female and sexually active, subject must be using a reliable form of birth control, be surgically sterile, or be at least 2 years post-menopausal).
k. Have a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to the baseline evaluation.
l. Be concomitantly participating in another clinical study.
m. Be involved in an injury claim under current litigation or have pending/approved worker's compensation claim.

n. Had surgery and/or interventional procedure to treat back and/or leg pain within 90 days (if surgery) and 30 days (if any other procedure) prior to the baseline evaluation.
o. Subject is a prisoner.
p. Being treated with electroconvulsive therapy (ECT) or transcranial magnetic stimulation (rTMS).
q. Subject is unwilling or unable to discontinue and remain off of any medication used to treat chronic pain that is not FDA approved for chronic pain.
r. Subject has pain due to peripheral vascular disease or angina.
s. Subject is on anticoagulation therapy that would preclude their ability to undergo the implant procedure.

Follow-up Schedule

All subjects first underwent a trial with the external trial stimulator to determine eligibility for the permanent implant. Randomization occurred following trial lead placement. Subjects who had at least a 50% reduction compared to baseline in overall trunk and limb pain as measured by a Visual Analog Scale (VAS) at the end of the trial were approved to receive a permanent implant. Other preoperative assessments are described in Table II.1. All subjects were scheduled to return postoperatively at 1-, 3-, 6-, 9-, and 12-months after implantation and biannually thereafter for up to 3 years. Postoperative assessments are described in Table II.2. Adverse events and complications were recorded at all visits. The key timepoints are shown below in the tables summarizing safety and effectiveness.

Table II.1. Pre- and Intraoperative Visit Schedule (Baseline through Implant Procedure)

Assessment	Screening/ Baseline	Trial Procedure	Trial End (≤30 days)	Implant Procedure (Day 0)
Informed Consent	X			
Inclusion/Exclusion	X			
Baseline Evaluation (Demographics, Medical History, Physical Exam, Psychological Evaluation)	X			
Pain Medication/ Therapies	X	X	X	X
Procedure/X-rays		X	[X]	X
Programming		X		X
Pain Assessment (Visual Analog Scale (VAS) & Pain Map)	X		X	
Pain Diary	X			
Oswestry Disability Index (ODI)	X			
Short Form Health Survey (SF-12)	X			
EQ-5D-5L	X			
Profile of Mood States (POMS)	X			
Pittsburgh Sleep Quality Index (PSQI)	X			
Adverse Event Monitoring	X	X	X	X
Study Exit			X[1]	

[X] = Optional
[1]A Study Exit form was completed for all enrolled (i.e., randomized) subjects at the time of study exit (i.e., study completion or early withdrawal).

Table II.2. Postoperative Visit Schedule (Follow-up)

Assessment	1 Month[1]	3 Month[1]	6 Month[1]	9 Month[1]	12 Month[1]	18, 24, 30, & 36 Month[1]
Telephone Follow-up	X	X	X	X	X	X
Pain Medication/ Therapies	X	X	X	X	X	X
Procedure/X-rays	[X]	[X]	[X]	[X]	[X]	[X]
Programming	[X]	[X]	[X]	[X]	[X]	[X]
Pain Assessment (Visual Analog Scale (VAS) & Pain Map)	X	X	X	X	X	X
Pain Diary	X	X	X		X	X
Oswestry Disability Index (ODI)	X	X	X		X	X
Short Form Health Survey (SF-12)	X	X	X		X	X
EQ-5D-5L	X	X	X		X	X
Profile of Mood States (POMS)	X	X	X		X	X
Pittsburgh Sleep Quality Index (PSQI)	X	X	X		X	X
Patient Global Impression of Change (PGIC) & Patient Satisfaction	X	X	X		X	X
Posture Change Assessment	X	X	X		X	X
Stimulation Characteristics		X			X	X
Blinding Assessments		X			X	
Adverse Event Monitoring	X	X	X	X	X	X
Study Exit						X[2]

[X] = Optional
[1]Visit Windows: 1-Month (30 days ± 14 days), 3-Month (90 days ± 14 days), 6-Month (180 days ± 30 days), 9-Month (270 days ± 30 days), 12-Month (365 days ± 30 days), 18-month (545±90 days), 24-month (730±90 days), 30-month (910±90 days), and 36-month (1095±90 days)
[2]A Study Exit form was completed for all enrolled (i.e., randomized) subjects at the time of study exit (i.e., study completion or early withdrawal).

Clinical Endpoints

The primary endpoint was a composite of the percentage of subjects that experienced a 50% or greater reduction in average overall trunk and limb pain at the primary endpoint visit (3-month) and had no increase in baseline pain medications within 4 weeks of the primary endpoint visit.

The primary analysis was conducted at the 3-month follow-up and an additional pre-defined analysis was completed at the 12-month follow-up.

(1) Individual Subject Success

An individual subject was considered a primary composite endpoint success if the subject:

- Experienced at least 50% pain relief in average overall trunk and limb pain as measured by a 100 mm Visual Analogue Scale (VAS) at 3-month visit; and
- No increase in baseline pain medications within 4 weeks of the primary endpoint visit.

Subjects who increase their baseline pain medications under the following conditions were considered a failure for this component of the primary endpoint:

- An increase in morphine equivalent units (MEU) of a baseline opioid within 4 weeks of primary endpoint visit.
  - Exceptions: temporary increase to treat post-procedure pain or an acute co-morbidity unrelated to the study indication that was not expected to respond to SCS.
- An increase from baseline in non-opiate pain medication used to treat their study indication pain for a duration of greater than 5 days that was not stopped within 4 weeks of primary endpoint visit.
  - Exceptions: Tylenol/rescue medication was allowed up to two weeks prior to the primary endpoint visit.

(2) Study Success

Study success was defined as the percentage of subjects who met the criteria for Individual Subject Success in the closed-loop (Investigational) group compared to the open-loop (Control) group, using a 10% non-inferiority margin. If non-inferiority was achieved at a one-sided alpha of 0.05, a two-sided superiority test was performed at the significance level of 0.05.

(3) Hierarchical Secondary Endpoints

If non-inferiority was met in the testing of the primary composite endpoint, the following secondary endpoints were successively evaluated (hierarchical test approach) in the order shown using a 10% non-inferiority margin with a 0.05 significance level until statistical significance was not achieved. All four secondary endpoints were initially tested at 3 months. If all four secondary endpoints passed non-inferiority at the 3-month analysis, hierarchical testing continued at 12 months in the same order specified below until a hypothesis test failed. All secondary endpoints that passed their non-inferiority test were tested for superiority, first at 3-months and then at 12-months. P-values adjusted for multiple comparisons (via the Hochberg method) are provided for the tests of superiority.

a. Comparison of percentage change from baseline in average leg pain (as assessed by VAS) between Investigational and Control groups at the primary endpoint visit.

b. Comparison of percentage change from baseline in average back pain (as assessed by VAS) between Investigational and Control groups at the primary endpoint visit.

c. Comparison of incidence of ≥80% reduction in average overall trunk and limb pain (as assessed by VAS) between Investigational and Control groups at the primary endpoint visit.

d. Comparison of incidence of ≥50% reduction in average back pain (as assessed by VAS) between Investigational and Control groups at the primary endpoint visit.

(4) Additional Secondary Endpoints

A number of additional secondary endpoints were also collected and assessed across study visits. These endpoints include the following:

a. Comprehensive summary of all Adverse Events (AEs)

b. Change, percent change, incidence of ≥50% (“responders”) and ≥80% (“high responders”) reduction, and cumulative proportion of responders analysis in VAS pain scores

c. Pain Map

   Data were collected by asking subjects to shade in the areas where they were experiencing pain on a body map drawing. These data were used to record the location of the pain being treated with the SCS system.

d. Pain Diary

   Data on pain variability were collected through subject completion of a pain diary.

e. Oswestry Disability Index (ODI)

f. Short Form Health Survey (SF-12)

g. EQ-5D-5L

h. Profile of Mood States Brief (POMS)

i. Pittsburgh Sleep Quality Index (PSQI)

j. Patient Global Impression of Change (PGIC)

   Data on patient global impression of change were collected as a single item measure of global improvement with treatment using a 7-point rating scale containing the options “very much improved”, “much improved”, “minimally improved”, “no change”, “minimally worse”, “much worse”, and “very much worse”.

k. Patient Satisfaction

   Data on subject satisfaction with the therapy and pain relief (“very satisfied,” “satisfied,” “neither satisfied nor unsatisfied,” “unsatisfied,” and “very unsatisfied”) along with likelihood of recommending the therapy (“strongly recommend,” “recommend,” “neutral,” “not recommend,” and “definitely not recommend”) were collected.

l. Posture Change Assessment

   Data on spinal cord (SC) activation (ECAP amplitude) and the subjects’ perception of stimulation intensity (11-point numeric scale, from 0 representing “No Feeling” to 10 “Very Intense” based on a published paresthesia intensity rating scale (1)) were collected in different postures in-clinic to mimic activities of daily living (i.e., coughing, lying down, and sitting).

m. Stimulation Characteristics

Data on subjects' general stimulation sensation and experience, including usage, perception of paresthesia, stimulation management strategies, and interaction with the device, were collected.

n. Programming and Neurophysiologic Properties

Programming parameters collected for each program during programming sessions included:

- Frequency (Hz)
- Pulse Width (µs)
- Stimulation Current Amplitude (mA)
- Measured Sensitivity (i.e., rate of change of the ECAP amplitude per unit input current (µV/mA))

Neurophysiological properties collected during programming sessions included:

- ECAP waveform features: ECAP amplitude, width, slope, and shape.
- Conduction Velocity: the speed at which an ECAP propagates along a neural pathway (m/s).
- Rheobase: the minimum stimulus current needed for neural activation at an infinitely long pulse width (mA).
- Chronaxie: the minimum pulse width needed for neural activation at twice the rheobase current (µs).
- Late Responses: neural responses resulting from dorsal root activation.

The ECAP amplitude is representative of the number of spinal cord (SC) fibers activated by stimulation (2). The Evoke System produces an ECAP amplitude for each stimulus and stores the ECAP amplitudes as histogram data. The ECAP amplitude histograms are an objective measure of the SC activation in response to spinal cord stimulation over time. The ECAP amplitude histograms were characterized by some key statistics to elucidate any differences in SC activation between closed-loop (Investigational) and open-loop (Control) stimulation. These include:

- Mode ECAP Amplitude: is a measure of the most frequent SC activation level for a given histogram period.
- Ratio of the Mode ECAP Amplitude to the Comfort Level ECAP Amplitude (mode/comfort level): is a measure of how close the most frequent SC activation level is to the comfort level. A value closer to 1 is indicative of SC activation near or at the comfort level.
- Ratio of the Interdecile ECAP Amplitude Range to the Median ECAP Amplitude ((90th percentile – 10th percentile)/median): is a measure of the spread of the ECAP amplitude histogram where lower values mean that the spread of the distribution is tighter around the median.

The therapeutic range of SC activation is defined by the ECAP amplitudes between patient perception threshold and maximum (i.e., therapeutic window).

- Patient Perception Threshold: the SC activation level the patient first feels a change in sensation (e.g., paresthesia, pain relief).
- Comfort Level: the SC activation level perceived as comfortable by the patient.
- Maximum Level: the SC activation level the patient can withstand (or tolerate) for approximately one minute.

The percent time the subjects' SC activation was within the therapeutic window was calculated. Refer to Figure II.1 for theoretical examples of ECAP amplitude represented as histogram data (normal and non-normal distribution) and how statistical measures from these histograms may be used to describe SC activation for a patient.

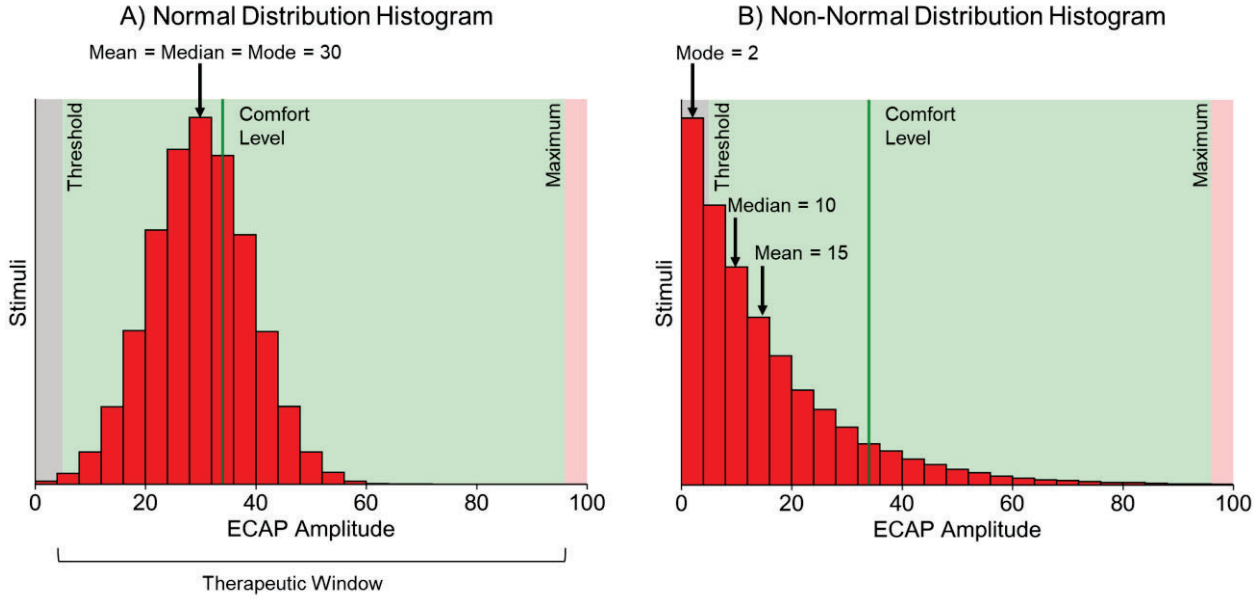


Figure II.1. Theoretical Examples of ECAP Amplitude Histogram Statistics

(5) Safety

The incidence and characteristics of all adverse events were evaluated for the entire study population and also compared between treatment groups.

(6) Analysis Populations

The primary analysis population, as prespecified in the Statistical Analysis Plan (SAP) was the Intention-To-Treat (ITT) analysis dataset, which included all randomized subjects with known endpoint status or classified as a presumed non-responder.

Additionally, the SAP prespecified an additional analysis population to assess study outcomes. The Permanent Implant Subset (PIS), a subset of the ITT analysis dataset, included the subjects in the ITT population who received a permanent implant.

The following events eliciting missing data at 3 months caused a subject to be classified as a presumed non-responder:

- Failure of the trial stimulation phase (<50% improvement in average overall trunk and limb pain VAS).
- Subject voluntary withdrawal due to an AE adjudicated as related to the device or stimulation.
- Investigator withdrawal due to an AE adjudicated as related to the device or stimulation.

Additionally, a subject was considered a presumed non-responder after 3 months if they withdrew due to lack of efficacy.

Presumed non-responders were analyzed as failures for the primary endpoint, hierarchical secondary endpoint, and other secondary endpoint VAS incidence measures. For hierarchical secondary endpoint and other secondary endpoint in-clinic VAS continuous measures, subjects with missing data categorized as presumed non-responders utilized a last-value carried forward imputation methodology. Subjects that failed the medication component of the primary endpoint had a change from baseline value of "0" imputed for the hierarchical secondary endpoint calculations.

2. Accountability of PMA Cohort

Patients were enrolled and randomized in the Evoke study between February 21, 2017 and February 20, 2018. The database for this PMA reflected data collected through April 1, 2019 and included 134 subjects (67 Investigational subjects, 67 Control subjects) from 13 investigational sites. All patients had passed through the 12-month window, and the study was in follow-up. The ITT population included 125 subjects (62 Investigational subjects, 63 Control subjects) at 3 months (timing of primary endpoint analysis) that were randomized and had known endpoint status (58 Investigational, 53 Control) or were classified as a presumed non-responder (4 Investigational, 10 Control), and 118 subjects at 12 months that were randomized and had known endpoint status (55 Investigational subjects, 48 Control subjects) or were classified as a presumed non-responder (4 Investigational subjects, 11 Control subjects).

Of the 125 subjects in the ITT population, 111 subjects (58 Investigational subjects, 53 Control subjects) received a permanent implant and were included in the PIS analysis set at 3 months. Fourteen randomized subjects failed the trial procedure (4 Investigational subjects, 10 Control subjects) and were therefore excluded from the PIS analysis dataset. At 12 months, there were 104 subjects (55 Investigational subjects, 49 Control subjects) in the PIS analysis dataset.

See Figure II.2 for a flow diagram of subject accountability.

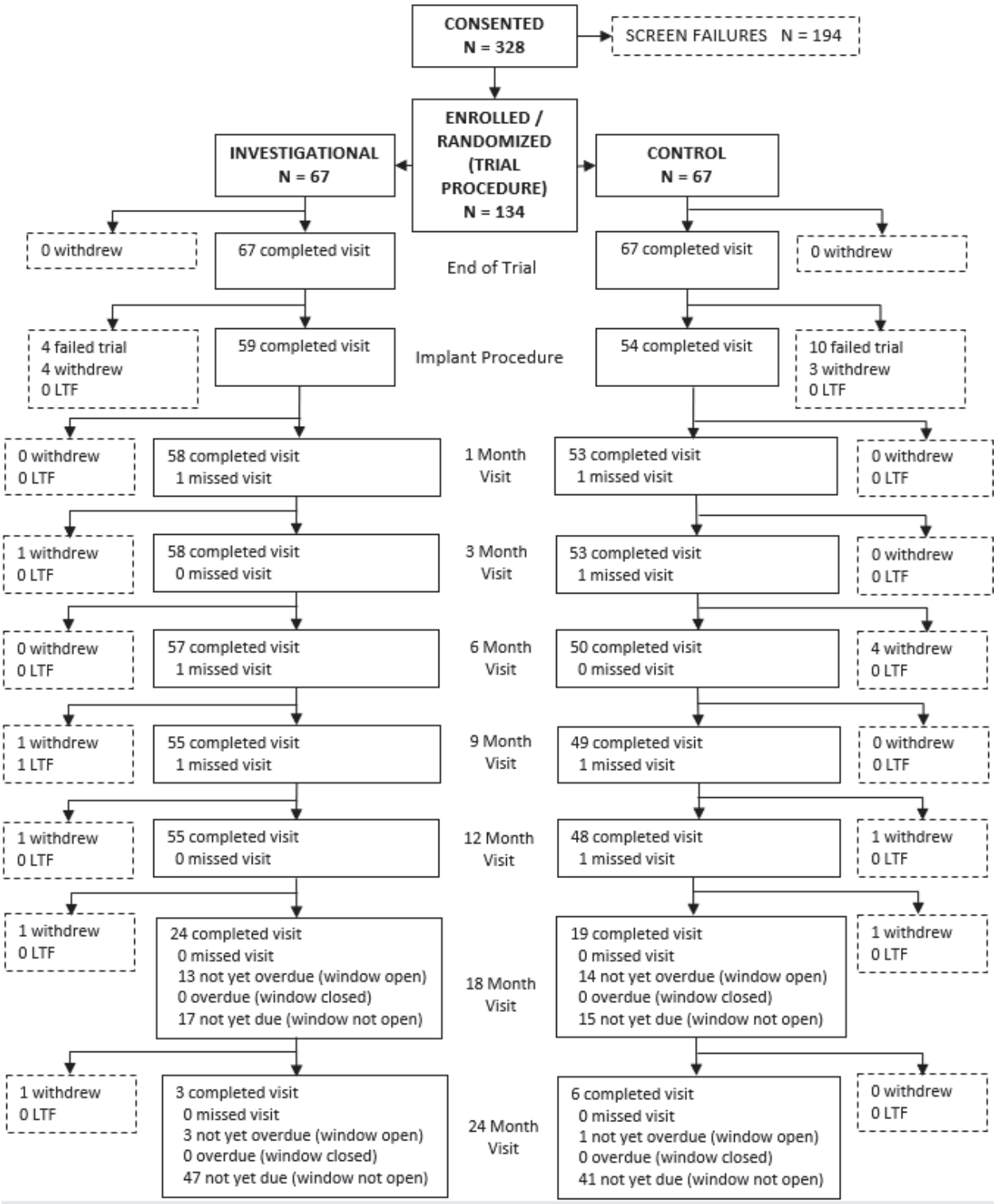


Figure II.2. Subject Accountability

3. Study Population Demographics and Baseline Parameters

Table II.3 presents information on key baseline demographics and characteristics. There were no statistically significant differences in baseline demographics and characteristics between treatment groups, indicating that the randomization resulted in balanced groups, supporting the validity of comparisons between the groups. The demographics of the study population are typical for a study of this type performed in the US.

Table II.3. Baseline Demographics and Characteristics – Randomized

Characteristic	Investigational N=67 Subjects	Control N=67 Subjects	P-value
Age (years)			
Mean (SD)	54.6 (9.7)	55.9 (11.6)	0.490
Min., Max.	28.7, 80.1	24.8, 80.8	
Gender (n (%))			
Male	34 (50.7%)	35 (52.2%)	1.000
Female	33 (49.3%)	32 (47.8%)	
Race (not mutually exclusive) (n (%))			
American Indian or Alaska Native	1 (1.5%)	2 (3.0%)	
Asian	0 (0.0%)	0 (0.0%)	
Black or African American	2 (3.0%)	6 (9.0%)	
Native Hawaiian or Other Pacific Islander	0 (0.0%)	0 (0.0%)	
White	63 (94.0%)	59 (88.1%)	0.365[1]
Other[2]	0 (0.0%)	2 (3.0%)	
Ethnicity (n (%))			
Hispanic/Latino	3 (4.5%)	6 (9.0%)	0.492
Non-Hispanic/Latino	64 (95.5%)	61 (91.0%)	
BMI (kg/m^2)			
Mean (SD)	31.3 (5.7)	32.4 (6.8)	0.335
Min., Max.	18.3, 46.2	17.5, 48.5	
Duration of Pain (years)			
Mean (SD)	13.6 (9.6)	11.2 (9.9)	0.151
Min., Max.	0.5, 41.4	0.7, 46.0	
Pain Location (n (%))			
Chronic Intractable Back Pain	67 (100%)	67 (100%)	
Chronic Intractable Leg Pain	67 (100%)	67 (100%)	
Unilateral	24 (35.8%)	28 (41.8%)	0.595[3]
Bilateral	43 (64.2%)	39 (58.2%)	
Pain Etiology (not mutually exclusive) (n (%))			
Arachnoiditis	0 (0.0%)	2 (3.0%)	0.496
Complex Regional Pain Syndrome (CRPS) I	0 (0.0%)	1 (1.5%)	1.000
Degenerative Disc Disease	33 (49.3%)	42 (62.7%)	0.164
Failed Back Surgery Syndrome (FBSS)	38 (56.7%)	41 (61.2%)	0.726
Internal Disc Disruption or Tear / Discogenic Pain	7 (10.4%)	10 (14.9%)	0.605
Lumbar Facet-Mediated Pain	8 (11.9%)	8 (11.9%)	1.000

Characteristic	Investigational N=67 Subjects	Control N=67 Subjects	P-value
Mild-Moderate Spinal Stenosis	26 (38.8%)	27 (40.3%)	1.000
Neuropathic Pain	1 (1.5%)	1 (1.5%)	1.000
Radiculopathy	61 (91.0%)	59 (88.1%)	0.779
Sacroiliac Joint-Mediated Pain	9 (13.4%)	5 (7.5%)	0.398
Spondylolisthesis	6 (9.0%)	5 (7.5%)	1.000
Spondylosis with Myelopathy	2 (3.0%)	3 (4.5%)	1.000
Spondylosis without Myelopathy	26 (38.8%)	24 (35.8%)	0.858
Other Chronic Pain	6 (9.0%)	3 (4.5%)	0.492
Baseline Pain Medication Usage	63 (94.0%)	59 (88.1%)	0.365
Opioids	41 (61.2%)	40 (59.7%)	1.000
Non-opioids[4]	51 (76.1%)	52 (77.6%)	1.000
Previous Non-Invasive Therapies[5]	65 (97.0%)	64 (95.5%)	1.000
Previous Interventional Procedure[6]	63 (94.0%)	62 (92.5%)	1.000
Previous Back Surgery[7]	39 (58.2%)	41 (61.2%)	0.860

Two-sample t-test between treatment groups for continuous variables; Fisher's exact test between treatment groups for categorical variables.
[1]Comparison of white versus non-white races.
[2]The 'Other' races included Middle Eastern (1) and Latino (1).
[3]Comparison of unilateral versus bilateral leg pain.
[4]Non-opioid pain medication classes include: anticonvulsant, antidepressant, local anesthetic, muscle relaxant, and NSAIDs
[5]Non-invasive therapies include: acupuncture, aquatherapy, assistive device, biofeedback, chiropractic care, exercise therapy, massage therapy, psychotherapy, physical therapy, transcutaneous electro-nerve stimulator (TENS)
[6]Interventional procedures include: ankle surgery, benign cyst removal, block/injection – other, epidural steroid injection, facet joint injection, intradiscal procedure (e.g., Intradiscal Electrothermal Therapy (IDET)), lumbar rhizotomy, lumbar sympathetic block, medial branch block, radiofrequency denervation, sacroiliac joint injection, trigger point injection
[7]Back surgeries include: artificial disc replacement, discectomy or microdiscectomy, foraminotomy, kyphoplasty and vertebroplasty, laminectomy, nucleoplasty (e.g., disc decompression, laser surgery), spinal fusion, back surgery – not otherwise specified, back surgery – other

Study Execution

Aside from the difference in stimulation mode, subjects in both treatment groups received the same care, with the device, implant procedure, and programming process being the same for both groups. There were no statistically significant differences between groups in procedure duration or lead placement for the trial or permanent implant procedures. All programming parameters were chosen using the process outlined in the Evoke Clinical Manual. Programming in both groups utilized ECAP measurement in addition to subject feedback to optimize patient outcomes. The only difference in programming was enabling (Investigational) or disabling (Control) the feedback loop. There were no statistically significant differences between groups in the frequency of programming visits, programming duration, and programming parameters (Table II.4). Both treatment groups used the device the majority of the time with no statistically significant differences in usage between groups.

Table II.4. Summary of Programming Parameters – ITT

Parameter	Investigational	Control	P-value
Stimulation Frequency (Hz)			
Mean (SD)	41.7 (16.6)	42.3 (13.6)	0.850
Min., Max.	10.0, 180.0	10.0, 90.0	

Parameter	Investigational	Control	P-value
Pulse Width (µs)			
Mean (SD)	308.9 (83.2)	296.9 (76.8)	0.660
Min., Max.	80.0, 740.0	100.0, 800.0	
Processing Offset (µs)			
Mean (SD)	182.9 (117.9)	176.7 (80.2)	0.662
Min., Max.	61.0, 2441.0	61.0, 610.0	
Filter Frequency (Hz)			
Mean (SD)	951.1 (135.9)	970.9 (182.8)	0.147
Min., Max.	565.0, 1928.0	565.0, 1928.0	
Patient Sensitivity* (µV/mA)			
Mean (SD)	98.9 (111.5)	--	--
Min., Max.	6.0, 1000.0	--	
Target Amplitude† (µV)			
Mean (SD)	49.5 (59.4)	--	--
Min., Max.	0.0, 348.1	--	

Repeated measures mixed model for difference between groups.
**Patient Sensitivity is used to set up the loop for the closed-loop (Investigational) therapy; is not relevant to the open-loop (Control) therapy.*
†Target Amplitude is set to the preferred level using the EPC during daily use by the patient for closed-loop (Investigational) therapy; is not relevant to the open-loop (Control) therapy. It is represented here by the Mode of the ECAP amplitude histogram collected prior to the 12-month visit.

Furthermore, at 3 and 12 months the subjects' electrophysiological measurements in both groups were statistically equivalent, demonstrating the ability of stimulation to recruit nerve fibers and produce action potentials (ECAP amplitude and other features), activate the same fiber types (conduction velocity), and produce comparable axonal excitability (rheobase) and membrane time constant (chronaxie) (Table II.5). These data indicate that the randomization generated directly comparable treatment groups with respect to neurophysiology. On average, the conduction velocity was approximately 60 m/s in both treatment groups, which is within the literature reported range for Aβ sensory fibers (3).

Table II.5. Summary of Neurophysiological Property Measurements at 3 and 12 Months – ITT

	3 Month			12 Month		
	Investigational	**Control**	**P-value**	**Investigational**	**Control**	**P-value**
Conduction Velocity (m/s)						
Median	57.3	58.9	0.430	60.2	58.9	0.996
Min., Max.	45.1, 93.2	42.0, 82.9		43.3, 84.2	45.2, 86.2	
Chronaxie (µs)						
Median	359.5	311.0	0.181	306.6	236.2	0.259
Min., Max.	75.7, 684.0	78.0, 866.7		116.9, 609.0	89.4, 633.4	
Rheobase (mA)						
Median	2.8	2.9	0.676	2.9	2.8	0.725
Min., Max.	0.7, 6.0	1.0, 9.9		1.1, 6.8	1.0, 6.9	

Kruskal-Wallis test between treatment groups.

Lastly, the double-blind design was maintained with no deviations in blinding, reducing the potential of data being systematically distorted by knowledge of the treatment received. The extent to which the characteristics of the treatment arms are statistically comparable and the robustness with which the study was executed and operationalized supports the strength of the study conclusions.

4. Safety and Effectiveness Results

Safety Results

The analysis of safety was based on all randomized subjects (134 subjects total; 67 Investigational subjects, 67 Control subjects), and included all adverse events reported and adjudicated as of database lock. On average, Investigational subjects had a permanent implant for 16.3 (±3.8) months and Control subjects had a permanent implant for 16.2 (±4.8) months (mean ± SD). The cumulative implant months of experience for subjects that received a permanent implant was 959.0 months (79.8 years) in the Investigational group and 874.9 months (72.8 years) in the Control group.

Key safety outcomes are presented below in Table II.6 through Table II.11.

As all subjects received the same investigational device, underwent the same trial and permanent implant procedures, and received active stimulation. The characteristics of the adverse events are presented by treatment group and treatment groups combined (total) (Table II.6), and by treatment groups combined only for the incidence of adverse event types (Table II.7 through Table II.11). Adverse events are reported according to the CEC adjudication. An adverse event was classified as 'study-related' if it was possibly or definitely related to the procedure, device, or stimulation therapy.

The characteristics of all adverse events occurring in the study are presented by treatment group and by treatment groups combined (total) in Table II.6. The type, nature, and severity of adverse events were similar between groups. No unanticipated serious adverse device effects (UADEs) occurred in this study as of database lock. There has been one death (cardiac arrest), unrelated to the study.

Table II.6. Characteristics of All Adverse Events – Randomized

	Investigational N=67 Subjects		Control N=67 Subjects		TOTAL N=134 Subjects	
Characteristic	Events n	Subjects n (%)	Events n	Subjects n (%)	Events n	Subjects n (%)
Total Adverse Events	**150**	**45 (67.2%)**	**104**	**45 (67.2%)**	**254**	**90 (67.2%)**
Serious						
No	134	42 (62.7%)	93	43 (64.2%)	227	85 (63.4%)
Study-related	22	12 (17.9%)	9	9 (13.4%)	31	21 (15.7%)
Yes	16	10 (14.9%)	11	8 (11.9%)	27	18 (13.4%)
Study-related	1	1 (1.5%)	2	2 (3.0%)	3	3 (2.2%)
Relation to Device						
Unrelated	143	45 (67.2%)	99	44 (65.7%)	242	89 (66.4%)
Possible	4	4 (6.0%)	3	3 (4.5%)	7	7 (5.2%)

Characteristic	Investigational N=67 Subjects		Control N=67 Subjects		TOTAL N=134 Subjects	
	Events n	Subjects n (%)	Events n	Subjects n (%)	Events n	Subjects n (%)
Definite	3	3 (4.5%)	2	2 (3.0%)	5	5 (3.7%)
Relation to Procedure						
Unrelated	133	44 (65.7%)	96	41 (61.2%)	229	85 (63.4%)
Possible	4	3 (4.5%)	3	3 (4.5%)	7	6 (4.5%)
Definite	13	9 (13.4%)	5	5 (7.5%)	18	14 (10.4%)
Relation to Stimulation Therapy						
Unrelated	145	44 (65.7%)	101	43 (64.2%)	246	87 (64.9%)
Possible	4	3 (4.5%)	2	2 (3.0%)	6	5 (3.7%)
Definite	1	1 (1.5%)	1	1 (1.5%)	2	2 (1.5%)
Severity						
Mild	41	27 (40.3%)	32	24 (35.8%)	73	51 (38.1%)
Moderate	87	37 (55.2%)	59	34 (50.7%)	146	71 (53.0%)
Severe	22	14 (20.9%)	13	9 (13.4%)	35	23 (17.2%)
Phase at Onset						
Prior to Trial	5	5 (7.5%)	3	3 (4.5%)	8	8 (6.0%)
Trial Period	1	1 (1.5%)	2	2 (3.0%)	3	3 (2.2%)
End of Trial to Implant	7	6 (9.0%)	6	5 (7.5%)	13	11 (8.2%)
Implant to 30 Days	12	11 (16.4%)	9	7 (10.4%)	21	18 (13.4%)
>30 days to 90 Days	26	17 (25.4%)	20	19 (28.4%)	46	36 (26.9%)
>90 Days to 365 Days	68	33 (49.3%)	51	29 (43.3%)	119	62 (46.3%)
>365 Days	31	16 (23.9%)	13	11 (16.4%)	44	27 (20.1%)
Outcome						
Ongoing	36	22 (32.8%)	28	21 (31.3%)	64	43 (32.1%)
Resolved without sequelae	99	35 (52.2%)	62	33 (49.3%)	161	68 (50.7%)
Resolved with sequelae	15	10 (14.9%)	14	9 (13.4%)	29	19 (14.2%)
Unanticipated Adverse Device Effect (UADE)[1]	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**

[1]An unanticipated adverse device effect (UADE) was defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

(1) Serious Adverse Events

Table II.7 presents the study-related serious adverse events by treatment groups combined (total). Three serious adverse events in three subjects (1 Investigational and 2 Control) were study-related (2.2%); none were stimulation related. All three serious study-related serious adverse events occurred within 30 days of the procedure. These events included wound infection, epidural abscess, and lead breakage/fracture.

Table II.7. Summary of Study-Related Serious Adverse Events – Randomized

	Total N=134 Subjects	
Preferred Term	**Events n**	**Subjects n (%)**
Total Adverse Events	**3**	**3 (2.2%)**
Epidural Abscess	1	1 (0.7%)
Lead Breakage/Fracture	1	1 (0.7%)
Wound Infection	1	1 (0.7%)

Table II.8 presents the serious adverse events by treatment groups combined (total). Among the 134 randomized subjects, a total of 27 serious adverse events (SAEs) in 18 subjects (13.4%) were reported (16 SAEs, 14.9% Investigational subjects; 11 SAEs, 11.9% Control subjects). Eighteen of the 27 (66.7%) serious adverse events were classified as severe. At the time of database lock three SAEs were still ongoing (3/27 = 11.1%).

Table II.8. Summary of Serious Adverse Events – Randomized

	Total N=134 Subjects	
Preferred Term	**Events n**	**Subjects n (%)**
Total Adverse Events	**27**	**18 (13.4%)**
Cellulitis	3	2 (1.5%)
Arrhythmia and Irregularities	2	2 (1.5%)
Abdominal Pain	1	1 (0.7%)
Anxiety Disorders	1	1 (0.7%)
Arthritis	1	1 (0.7%)
Benign Prostatic Hypertrophy	1	1 (0.7%)
Cardiac Chest Pain	1	1 (0.7%)
Cholecystitis	1	1 (0.7%)
Coronary Artery or Heart Disease	1	1 (0.7%)
Dehydration	1	1 (0.7%)
Diverticulitis	1	1 (0.7%)
Epidural Abscess	1	1 (0.7%)
Facet Cyst	1	1 (0.7%)
Fall or Trip or Slip or Twist	1	1 (0.7%)
Lead Breakage/Fracture	1	1 (0.7%)
Liver Abscess	1	1 (0.7%)
MRSA	1	1 (0.7%)
Myocardial Infarct or Heart Attack	1	1 (0.7%)
Peripheral Vascular Disease	1	1 (0.7%)
Prostate Cancer	1	1 (0.7%)
Renal Insufficiency	1	1 (0.7%)
Suicidal Ideation or Attempt	1	1 (0.7%)
Transient Ischemic Attack	1	1 (0.7%)
Wound Infection	1	1 (0.7%)

(2) All Adverse Events

Table II.9 presents the study-related adverse events by treatment groups combined (total). There were no differences between treatment groups in study-related (device, procedure and/or stimulation therapy) adverse events. As both treatment groups received the same device and underwent the same procedure, as expected there were no differences between groups in device- and procedure-related adverse events. Importantly, there were no differences in stimulation therapy-related adverse events.

Among the 134 randomized subjects, a total of 34 study-related adverse events (AEs) in 24 subjects (17.9%) were reported. The Investigational group had 23 study-related adverse events in 13 subjects (19.4%; 95% CI: 10.8, 30.9) and the Control group had 11 study-related adverse events in 11 subjects (16.4%; 95% CI: 8.5, 27.5). The most frequently reported study-related adverse events in both treatment groups were lead migrations (6.7%), IPG pocket pain (3.7%), and muscle spasm or cramp (2.2%). There were five stimulation therapy-related events in four Investigational subjects (6.0%; 95% CI: 1.7, 14.6) and three stimulation therapy-related events in three Control subjects (4.5%; 95% CI: 0.9, 12.5).

Table II.9. Summary of Study-Related Adverse Events – Randomized

	Total N=134 Subjects	
Preferred Term	**Events n**	**Subjects n (%)**
Total Adverse Events	**34**	**24 (17.9%)**
Lead Migration	10	9 (6.7%)
IPG Pocket Pain	5	5 (3.7%)
Muscle Spasm or Muscle Cramp	3	3 (2.2%)
Dural Puncture or Tear	2	2 (1.5%)
IPG Malfunction due to Electrocautery	2	2 (1.5%)
Unwanted Stimulation Location	2	2 (1.5%)
Wound Infection	2	2 (1.5%)
Dysesthesia - Lower Extremity	1	1 (0.7%)
Epidural Abscess	1	1 (0.7%)
Inadequate Lead Placement	1	1 (0.7%)
Lead Breakage/Fracture	1	1 (0.7%)
Low Back Pain	1	1 (0.7%)
Nausea and/or vomiting	1	1 (0.7%)
Skin Irritation or Redness	1	1 (0.7%)
Wound Dehiscence	1	1 (0.7%)

Table II.10 presents all adverse events for treatment groups combined (total). Among the 134 randomized subjects, a total of 254 adverse events (AEs) in 90 subjects (67.2%) were reported (150 AEs, 67.2% Investigational subjects; 104 AEs, 67.2% Control subjects). The majority of all adverse events (219/254 = 86.2%) were classified as mild or moderate in severity with only 13.8% (35/254)

being considered severe for 23 subjects (17.2%). At the time of database lock, of the 254 adverse events, 64 were still ongoing (25.2%), and 190 AEs were resolved (74.8%).

Table II.10. Summary of All Adverse Events – Randomized

	Total N=134 Subjects	
Preferred Term	Events n	Subjects n (%)
Total Adverse Events	**254**	**90 (67.2%)**
Fall or Trip or Slip or Twist	22	18 (13.4%)
Upper Respiratory Symptoms or Upper Respiratory Tract Infection	18	14 (10.4%)
Lead Migration	10	9 (6.7%)
Bronchitis	6	5 (3.7%)
IPG Pocket Pain	5	5 (3.7%)
Bursitis	5	4 (3.0%)
Cellulitis	5	4 (3.0%)
Motor Vehicle Accident	5	4 (3.0%)
Sinus Infection or Sinusitis	5	4 (3.0%)
Anxiety Disorders	4	4 (3.0%)
Ear Infection	4	4 (3.0%)
Unilateral Leg Pain	4	4 (3.0%)
Nausea and/or vomiting	4	3 (2.2%)
Abdominal Pain	3	3 (2.2%)
Arrhythmia and Irregularities	3	3 (2.2%)
Arthritis	3	3 (2.2%)
Hip Joint Pain	3	3 (2.2%)
Muscle Spasm or Muscle Cramp	3	3 (2.2%)
Peripheral Neuropathy - Lower Extremity	3	3 (2.2%)
Radiculopathy - Lower Extremity	3	3 (2.2%)
Upper Extremity Pain	3	3 (2.2%)
Activities of Daily Living (ADL) Injury	3	2 (1.5%)
Knee Pain	3	2 (1.5%)
Abnormal Blood Chemistry	2	2 (1.5%)
Bladder Infection	2	2 (1.5%)
Bone Fracture	2	2 (1.5%)
Bone Spur	2	2 (1.5%)
Cardiac Chest Pain	2	2 (1.5%)
Dental Issues	2	2 (1.5%)
Diarrhea	2	2 (1.5%)
Disc Bulge or Protrusion	2	2 (1.5%)
Dural Puncture or Tear	2	2 (1.5%)
Dysesthesia - Lower Extremity	2	2 (1.5%)
Facet joint deterioration	2	2 (1.5%)
Foot Pain	2	2 (1.5%)
Gastroenteritis	2	2 (1.5%)

	Total N=134 Subjects	
Preferred Term	Events n	Subjects n (%)
Headache	2	2 (1.5%)
IPG Malfunction due to Electrocautery	2	2 (1.5%)
Neck or Cervical Pain	2	2 (1.5%)
Peripheral Vascular Disease	2	2 (1.5%)
Prostate Cancer	2	2 (1.5%)
Pulled or Strained Muscle	2	2 (1.5%)
Restless Leg Syndrome	2	2 (1.5%)
SI Joint Pain	2	2 (1.5%)
Sacroiliitis	2	2 (1.5%)
Skin Infection	2	2 (1.5%)
Skin Rash	2	2 (1.5%)
Spinal Stenosis	2	2 (1.5%)
Syncope or Fainting	2	2 (1.5%)
Tremor - Upper Extremity	2	2 (1.5%)
Trigger Finger or Stenosing Tenosynovitis	2	2 (1.5%)
Unwanted Stimulation Location	2	2 (1.5%)
Wound Infection	2	2 (1.5%)
Back Pain and Bilateral Radiation into Legs	2	1 (0.7%)
MRSA	2	1 (0.7%)
Abnormal Uterine Bleeding	1	1 (0.7%)
Acne	1	1 (0.7%)
Adrenal Nodule	1	1 (0.7%)
Alopecia	1	1 (0.7%)
Ankylosing Spondylitis	1	1 (0.7%)
Back Pain	1	1 (0.7%)
Back and Upper Extremities Pain	1	1 (0.7%)
Benign Prostatic Hypertrophy	1	1 (0.7%)
COPD (Chronic Obstructive Pulmonary Disease)	1	1 (0.7%)
Cholecystitis	1	1 (0.7%)
Chronic Pain Syndrome	1	1 (0.7%)
Cirrhosis or Fatty Liver	1	1 (0.7%)
Coccydynia	1	1 (0.7%)
Coronary Artery or Heart Disease	1	1 (0.7%)
Dehydration	1	1 (0.7%)
Diverticulitis	1	1 (0.7%)
Diverticulosis	1	1 (0.7%)
Edema - Lower Extremities	1	1 (0.7%)
Epidural Abscess	1	1 (0.7%)
Erythema	1	1 (0.7%)
Eye Infection	1	1 (0.7%)
Eye Injury or Pain	1	1 (0.7%)

	Total N=134 Subjects	
Preferred Term	Events n	Subjects n (%)
Facet Cyst	1	1 (0.7%)
Fibromyalgia	1	1 (0.7%)
Forgetfulness or Memory Loss	1	1 (0.7%)
Gastritis	1	1 (0.7%)
Hypertension	1	1 (0.7%)
Impaired Balance	1	1 (0.7%)
Inadequate Lead Placement	1	1 (0.7%)
Incontinence	1	1 (0.7%)
Joint Disorders or Injury	1	1 (0.7%)
Kidney Stone	1	1 (0.7%)
Lead Breakage/Fracture	1	1 (0.7%)
Leukemia	1	1 (0.7%)
Liver Abscess	1	1 (0.7%)
Low Back Pain	1	1 (0.7%)
Lytic Lesion(s)	1	1 (0.7%)
Macromastia	1	1 (0.7%)
Migraine	1	1 (0.7%)
Myocardial Infarct or Heart Attack	1	1 (0.7%)
Myofascial Pain Syndrome	1	1 (0.7%)
Osteoporosis	1	1 (0.7%)
Overdose	1	1 (0.7%)
Peripheral Neuropathy - Upper Extremity	1	1 (0.7%)
Plantar fasciitis	1	1 (0.7%)
Pneumonia	1	1 (0.7%)
Radiculopathy - Upper Extremity	1	1 (0.7%)
Renal Cyst	1	1 (0.7%)
Renal Insufficiency	1	1 (0.7%)
Shingles	1	1 (0.7%)
Sinus Problems - Other	1	1 (0.7%)
Skin Irritation or Redness	1	1 (0.7%)
Strep Throat	1	1 (0.7%)
Stroke	1	1 (0.7%)
Suicidal Ideation or Attempt	1	1 (0.7%)
Throat Adenoma NOS	1	1 (0.7%)
Thryoid Adenoma	1	1 (0.7%)
Tinnitis	1	1 (0.7%)
Tooth Infection	1	1 (0.7%)
Transient Ischemic Attack	1	1 (0.7%)
Weakness - Lower Extremity	1	1 (0.7%)
Weakness - Upper Extremity	1	1 (0.7%)
Wound Dehiscence	1	1 (0.7%)

(3) Subsequent Surgical Procedures

Table II.11 presents a summary of implanted device replacements, revisions, and explants by treatment groups combined (total). There were a total of 22 subsequent surgical procedures; 13 procedures in nine Investigational subjects and nine procedures in eight Control subjects. Four Investigational subjects and five Control subjects underwent system explants. All nine subjects exited the study following explant.

Table II.11. Subsequent Revision, Replacement, or Explant Procedures – Randomized

	Total N=134 subjects	
Subsequent Procedure	**Events N**	**Subjects n (%)**
Revision - Implant Phase		
Lead(s)	1	1 (0.7%)
CLS	1	1 (0.7%)
System	1	1 (0.7%)
Replacement - Implant Phase		
Lead(s)	7	7 (5.2%)
CLS	2	2 (1.5%)
System	1	1 (0.7%)
System Explant - Implant Phase[1]	**9**	**9 (6.7%)**

[1]Reasons for system explant included: wound infection, epidural abscess, lead migration resulting in physician order to replace with paddle lead (Saluda Medical paddle lead not yet available), required MRI, lack of efficacy, and patient request.

Effectiveness Results

The analysis of effectiveness was based on the ITT population. The primary analysis occurred at 3 months and included 125 subjects total (62 Investigational subjects, 63 Control subjects). An additional analysis was completed at 12 months and included 118 subjects total (59 Investigational subjects, 59 control subjects). Key effectiveness outcomes are presented below in Table II.12 through Table II.19.

(1) Primary Composite Endpoint Primary (ITT) Analysis

The primary composite endpoint, which assessed pain improvement without increase in baseline pain medications, successfully demonstrated non-inferiority (prespecified 10% non-inferiority margin; p-value < 0.001) of closed-loop stimulation (Investigational) to open-loop stimulation (Control) (Table II.12 and Figure II.3) at 3 and 12 months. In total, 82.3% of Investigational subjects compared to 60.3% of the Control subjects at 3 months, and 83.1% of Investigational subjects compared to 61.0% of Control subjects at 12 months, met the criteria for Individual Subject Success. As non-inferiority was successfully established, superiority was also evaluated. The results of the study successfully demonstrated that closed-loop stimulation was superior to open-loop stimulation at 3 months (p-value = 0.005) and 12 months (p-value = 0.006).

Table II.12. Primary Composite Endpoint Treatment Success at 3 and 12 Months - ITT

	3 Month		12 Month	
Primary Endpoint Component	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - ITT	**62**	**63**	**59**	**59**
Overall Primary Endpoint Success				
n/N (%)	51/62 (82.3%)	38/63 (60.3%)	49/59 (83.1%)	36/59 (61.0%)
95% CI	(72.7%, 91.8%)	(48.2%, 72.4%)	(73.5%, 92.6%)	(48.6%, 73.5%)
Success rate difference (%) and 95% CI	21.9% (6.6%, 37.3%)		22.0% (6.3%, 37.7%)	
P-value (non-inferiority δ = 10%)	<0.001		<0.001	
P-value (superiority)	0.005		0.006	
Primary Endpoint Failures (n)	**11**	**25**	**10**	**23**
<50% overall trunk and limb pain relief at follow-up visit*	7	14	4	9
Increase in baseline pain medications within 4 weeks of the follow-up visit*	0	3	2	6
Presumed non-responders	4	10	4	11

**Not mutually exclusive.*
Normal approximation to binomial test.

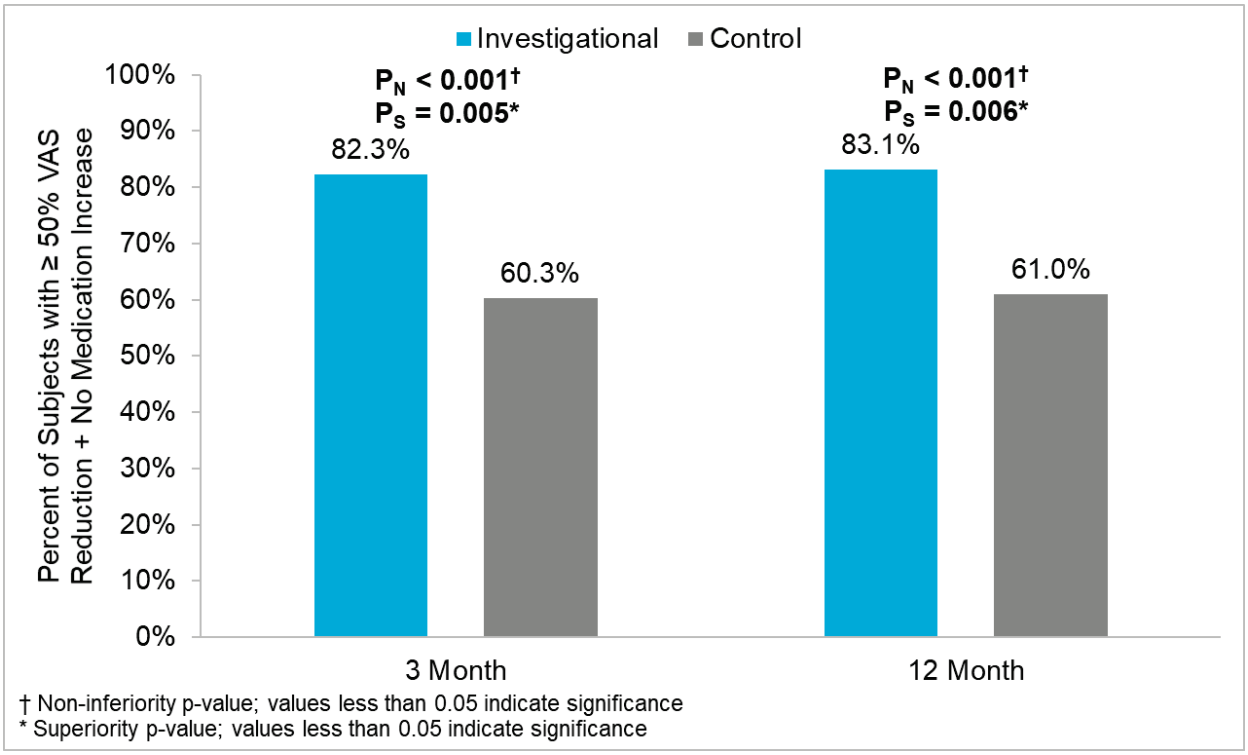


Figure II.3. Primary Composite Endpoint Treatment Success at 3 and 12 Months – ITT

(2) Primary Composite Endpoint PIS Analysis

As noted above, the primary composite endpoint was also assessed in the PIS analysis population. This analysis allowed for a more specific assessment of the performance of closed-loop stimulation in the group of study subjects who actually received the permanent implant and underwent the full course of treatment. In the PIS analysis population, 87.9% of Investigational subjects compared to 71.7% of Control subjects at 3 months, and 89.1% of Investigational subjects compared to 73.5% of Control subjects at 12 months, met the Individual Subject Success criteria (Table II.13). These results successfully demonstrated both non-inferiority (prespecified 10% non-inferiority margin; p-value <0.001) and superiority (3 months: p-value = 0.031; 12 months: p-value = 0.039) of closed-loop stimulation (Investigational) to open-loop stimulation (Control) at 3 and 12 months. The consistency of the outcomes of the primary endpoint analysis using the ITT population and the PIS population confirms the robustness of the study conclusions.

Table II.13. Primary Composite Endpoint Treatment Success at 3 and 12 Months - PIS

	3 Month		12 Month	
Primary Endpoint Component	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - PIS	**58**	**53**	**55**	**49**
Overall Primary Endpoint Success				
n/N (%)	51/58 (87.9%)	38/53 (71.7%)	49/55 (89.1%)	36/49 (73.5%)
95% CI	(79.5%, 96.3%)	(59.6%, 83.8%)	(80.9%, 97.3%)	(61.1%, 85.8%)
Success rate difference (%) and 95% CI	16.2% (1.5%, 31.0%)		15.6% (0.8%, 30.5%)	
P-value (non-inferiority δ = 10%)	<0.001		<0.001	
P-value (superiority)	0.031		0.039	
Primary Endpoint Failures (n)	**7**	**15**	**6**	**13**
<50% overall trunk and limb pain relief at follow-up visit*	7	14	4	9
Increase in baseline pain medications within 4 weeks of the follow-up visit*	0	3	2	6
Presumed non-responders	0	0	0	1

**Not mutually exclusive.*
Normal approximation to binomial test.

(3) Hierarchical Secondary Endpoints

All predefined, hierarchical secondary endpoints demonstrated non-inferiority of closed-loop (Investigational) to open-loop (Control) stimulation. While outcomes were also numerically better in the closed-loop group across all of these measures, closed-loop stimulation was statistically superior to open-loop stimulation in the percentage change in VAS average back pain at 3 months and the incidence of ≥50% reduction in VAS average back pain at 3 and 12 months. These results further support the robust pain improvements demonstrated by those treated with closed-loop stimulation, indicating that this form of stimulation provides a meaningful clinical benefit as compared to the existing, commercially available, SCS options.

The first hierarchical secondary endpoint, percentage change in VAS average leg pain, successfully demonstrated non-inferiority of closed-loop stimulation (Investigational) to open-loop stimulation (Control) at 3 and 12 months (prespecified 10% non-inferiority margin; p-value < 0.001) (Table II.14). Mean percentage change in VAS average leg pain was 76.8% in the Investigational group compared to 67.8% in the Control group at 3 months, and 72.9% in the Investigational group compared to 62.1% in the Control group at 12 months.

Table II.14. Percentage Change in VAS Average Leg Pain at 3 and 12 Months – ITT

	3 Month		12 Month	
Hierarchal Secondary Endpoint	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - ITT	**62**	**63**	**59**	**59**
Percent Reduction in VAS Leg Pain				
Mean (SD)	76.8 (28.3)	67.8 (35.5)	72.9 (31.0)	62.1 (37.5)
Median	87.9	81.7	85.6	75.4
Min., Max.	-10.4, 100.0	-9.1, 100.0	-10.4, 100.0	-6.4, 100.0
Difference between means and 95% CI	9.0 (-2.4, 20.4)		10.7 (-1.8, 23.3)	
P-value (non-inferiority δ = 10%)	<0.001		<0.001	
P-value (superiority, adjusted*)	0.119		0.093	

**Hochberg procedure.*
two-sample t-test

The second hierarchical secondary endpoint, percentage change in VAS average back pain, successfully demonstrated non-inferiority at 3 and 12 months (prespecified 10% non-inferiority margin; p-value < 0.001) and superiority at 3 months (p-value = 0.045) of closed-loop stimulation (Investigational) to open-loop stimulation (Control) (Table II.15). Mean percentage change in VAS average back pain was 72.1% in the Investigational group compared to 57.5% in the Control group at 3 months, and 69.4% in the Investigational group compared to 54.0% in the Control group at 12 months.

Table II.15. Percentage Change in VAS Average Back Pain at 3 and 12 Months – ITT

	3 Month		12 Month	
Hierarchal Secondary Endpoint	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - ITT	**62**	**63**	**59**	**59**
Percent Reduction in VAS Back Pain				
Mean (SD)	72.1 (29.4)	57.5 (36.4)	69.4 (30.6)	54.0 (39.5)
Median	85.4	64.9	81.1	62.7
Min., Max.	-4.2, 100.0	-16.2, 100.0	-4.2, 100.0	-16.2, 100.0
Difference between means and 95% CI	14.6 (2.9, 26.3)		15.4 (2.5, 28.3)	
P-value (non-inferiority δ = 10%)	<0.001		<0.001	
P-value (superiority, adjusted*)	0.045		0.059	

**Hochberg procedure.*
two-sample t-test

The third hierarchical secondary endpoint, incidence of ≥80% reduction (prespecified in the study protocol as high responders) in VAS average overall trunk and limb pain, successfully demonstrated non-inferiority of closed-loop stimulation (Investigational) to open-loop stimulation (Control) at 3

and 12 months (prespecified 10% non-inferiority margin; 3 months: p-value = 0.002; 12-months: p-value < 0.001) (Table II.16, Figure II.4, and Figure II.5). 58.1% of Investigational subjects compared to 42.9% of Control subjects met the endpoint at 3 months, and 55.9% of Investigational subjects compared to 37.3% of Control subjects met the endpoint at 12 months.

Table II.16. Incidence of ≥80% Reduction in VAS Average Overall Trunk and Limb Pain at 3 and 12 Months – ITT

	3 Month		12 Month	
Hierarchal Secondary Endpoint	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - ITT	**62**	**63**	**59**	**59**
Incidence of ≥ 80% Reduction in VAS Overall Trunk and Limb Pain				
n/N (%)	36/62 (58.1%)	27/63 (42.9%)	33/59 (55.9%)	22/59 (37.3%)
95% CI	(45.8%, 70.3%)	(30.6%, 55.1%)	(43.3%, 68.6%)	(24.9%, 49.6%)
Success rate difference (%) and 95% CI	15.2% (-2.1%, 32.5%)		18.6% (1.0%, 36.3%)	
P-value (non-inferiority δ = 10%)	0.002		<0.001	
P-value (superiority, adjusted*)	0.119		0.078	

**Hochberg procedure.*
normal approximation to binomial test

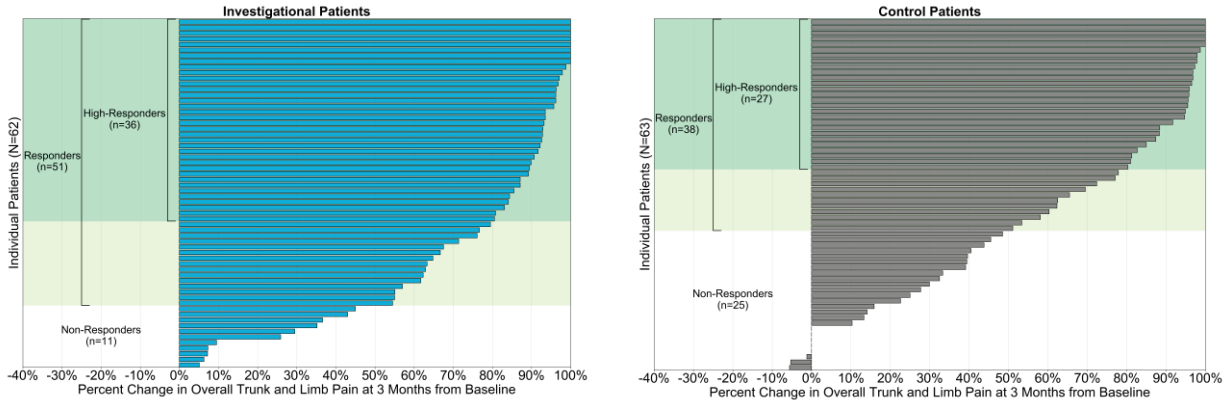


Figure II.4. Individual Percent Change from Baseline in In-Clinic VAS Average Overall Trunk and Limb Pain Scores at 3 Months – ITT

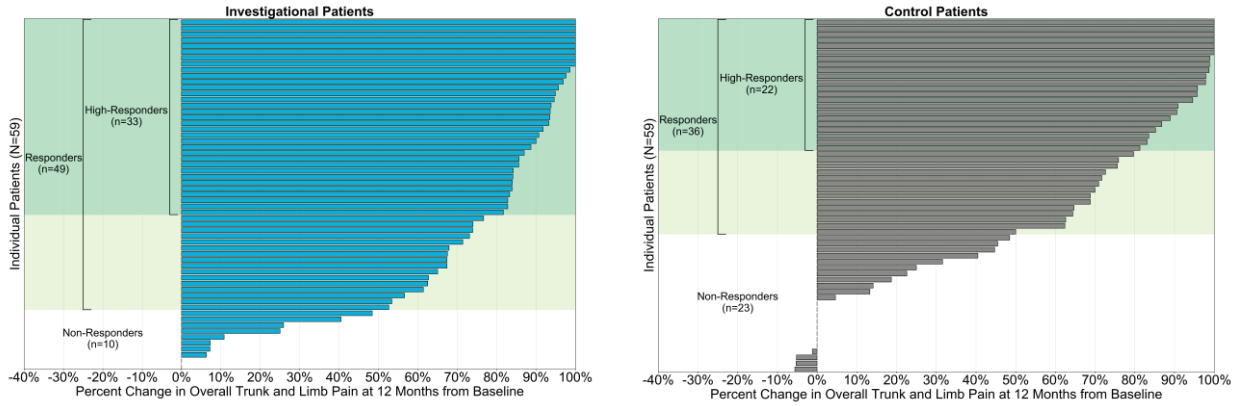


Figure II.5. Individual Percent Change from Baseline in In-Clinic VAS Average Overall Trunk and Limb Pain Scores at 12 Months – ITT

The fourth hierarchical secondary endpoint, incidence of ≥50% reduction (responder) in VAS average back pain, successfully demonstrated non-inferiority (prespecified 10% non-inferiority margin; p-value < 0.001) and superiority (3 months: p-value = 0.013; 12 months: p-value = 0.032) of closed-loop stimulation (Investigational) to open-loop stimulation (Control) at 3 and 12 months (Table II.17). 80.6% of Investigational subjects compared to 57.1% of Control subjects met the endpoint at 3 months, and 79.7% of Investigational subjects compared to 57.6% of Control subjects met the endpoint at 12 months.

Table II.17. Incidence of ≥50% Reduction in VAS Average Back Pain at 3 and 12 Months – ITT

	3 Month		12 Month	
Hierarchal Secondary Endpoint	**Investigational**	**Control**	**Investigational**	**Control**
Number of Subjects - ITT	**62**	**63**	**59**	**59**
Incidence of ≥ 50% Reduction in VAS Back Pain				
n/N (%)	50/62 (80.6%)	36/63 (57.1%)	47/59 (79.7%)	34/59 (57.6%)
95% CI	(70.8%, 90.5%)	(44.9%, 69.4%)	(69.4%, 89.9%)	(45.0%, 70.2%)
Success rate difference (%) and 95% CI	23.5% (7.8%, 39.2%)		22.0% (5.8%, 38.3%)	
P-value (non-inferiority δ = 10%)	<0.001		<0.001	
P-value (superiority, adjusted*)	0.013		0.032	

**Hochberg procedure.*
normal approximation to binomial test

(4) Additional Secondary Endpoints

A number of additional secondary endpoints were assessed and collectively provide increased evidence in support of the determination of effectiveness drawn from the assessment of the primary and hierarchical secondary endpoints. Table II.18 provides a summary of the additional

secondary endpoint analyses of patient reported outcome (PRO) measures collected in the Evoke study per the recommendations of IMMPACT (4,5) including pain intensity measured by VAS, functional disability measured by ODI, quality of life measured by SF-12 and EQ-5D-5L, emotional functioning measured by POMS, sleep measured by PSQI, impression of change measured by PGIC, and patient satisfaction. Numerically greater improvements were observed across these measures in the Investigational group, further supporting the conclusion of efficacy for the closed-loop treatment.

Table II.18. Summary Patient Reported Outcome (PRO) Measurements at 3 and 12 Months – ITT

	3 Month		12 Month	
	Investigational	**Control**	**Investigational**	**Control**
Responder Rates (% subjects)				
VAS Back Pain ≥80% Reduction	56.5%	36.5%	50.8%	35.6%
VAS Leg Pain ≥50% Reduction	80.6%	68.3%	83.1%	61.0%
VAS Leg Pain ≥80% Reduction	66.1%	54.0%	55.9%	47.5%
Percent Change from Baseline (mean (SD))[1]				
VAS Overall Pain	73.8 (28.0)	59.4 (35.8)	72.3 (29.0)	56.2 (38.5)
Change from Baseline (mean (SD))[1]				
ODI	30.3 (16.4)	26.5 (15.5)	28.0 (16.3)	26.1 (14.5)
SF-12 PCS	13.9 (9.8)	11.5 (9.4)	11.7 (10.6)	11.6 (9.6)
SF-12 MCS	8.9 (10.4)	1.9 (10.2)	7.4 (12.2)	-0.8 (10.0)
EQ-5D-5L Index Score	0.269 (0.172)	0.256 (0.162)	0.245 (0.194)	0.226 (0.170)
EQ VAS	28.3 (22.7)	22.0 (23.1)	27.1 (23.4)	20.3 (20.7)
POMS TMD	20.2 (21.2)	10.1 (14.1)	21.7 (19.8)	8.9 (14.6)
PSQI	5.7 (4.6)	4.5 (4.0)	5.7 (4.2)	4.5 (4.7)
Clinically Important Change (% subjects)				
ODI[2]	81.0%	79.2%	78.2%	77.1%
SF-12 PCS[3]	81.0%	66.0%	72.7%	72.9%
SF-12 MCS[3]	55.2%	28.3%	50.9%	20.8%
EQ-5D-5L Index Score[4]	89.7%	86.8%	85.5%	79.2%
POMS TMD[5]	69.0%	41.5%	70.9%	45.8%
PSQI[6]	75.9%	66.0%	76.4%	62.5%
Other (% subjects)				
ODI Percent Minimal to Moderate Disability[2]	84.5%	77.4%	80.0%	70.8%
Change from Baseline from PSQI Poor to Good Sleep Quality[7,8]	31.6%	28.8%	29.6%	27.7%
PGIC (% much improved or very much improved)	89.7%	81.1%	81.8%	75.0%

	3 Month		12 Month	
	Investigational	**Control**	**Investigational**	**Control**
Subject Satisfaction with Therapy (% satisfied or very satisfied)	94.8%	86.8%	90.9%	85.4%

Abbreviations: MCS = Mental Component Summary; ODI = Oswestry Disability Index; PCS = Physical Component Summary; PGIC = Patient Global Impression of Change; POMS = Profile of Mood States; PSQI = Pittsburgh Sleep Quality Index; SF-12 = Short Form Health Survey; TMD = Total Mood Disturbance; VAS = Visual Analog Scale

[1] Positive change is better.

[2] Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. Spine. 2000 Dec 15;25(24):3115-24.

[3] Maruish, M. E. (Ed.). (2012). User's manual for the SF-12v2 Health Survey (3rd ed.). Lincoln, RI: QualityMetric Incorporated.

[4] Walters, S. J. & Brazier, J. E. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. Quality of Life Research 14, 1523-1532 (2005).

[5] Dworkin, R. H. et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. J Pai n 9, 105-121 (2008).

[6] Buysse, D. J. et al. Efficacy of brief behavioral treatment for chronic insomnia in older adults. Arch. Intern. Med. 171, 887-895 (2011).

[7] Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R. & Kupfer, D. J. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28, 193-213 (1989).

[8] Does not include subjects who did not qualify for the Baseline condition or who did not have a follow-up.

Mode of Action

The working hypothesis of the mechanism of action of SCS postulates that ascending pain signals can be inhibited by activity generated in low threshold sensory fibers within the spinal cord (SC) (e.g., Aβ-fibers), which are the target of SCS. These fibers synapse with interneurons in the dorsal horn that provide inhibitory input to wide dynamic range (WDR) neurons. The limitation of open-loop SCS systems is the lack of adjustment to the broad range of electrical field strength reaching the SC due to changes in distance between the stimulation electrode and the SC. This is caused by normal physiological activity (e.g., breathing and heartbeat) and movement, which results in variable SC activation (6–9). The mode of action of the Evoke System addresses this challenge using ECAP-controlled closed-loop SCS which automatically adjusts the stimulation current in real-time to maintain consistent SC activation.

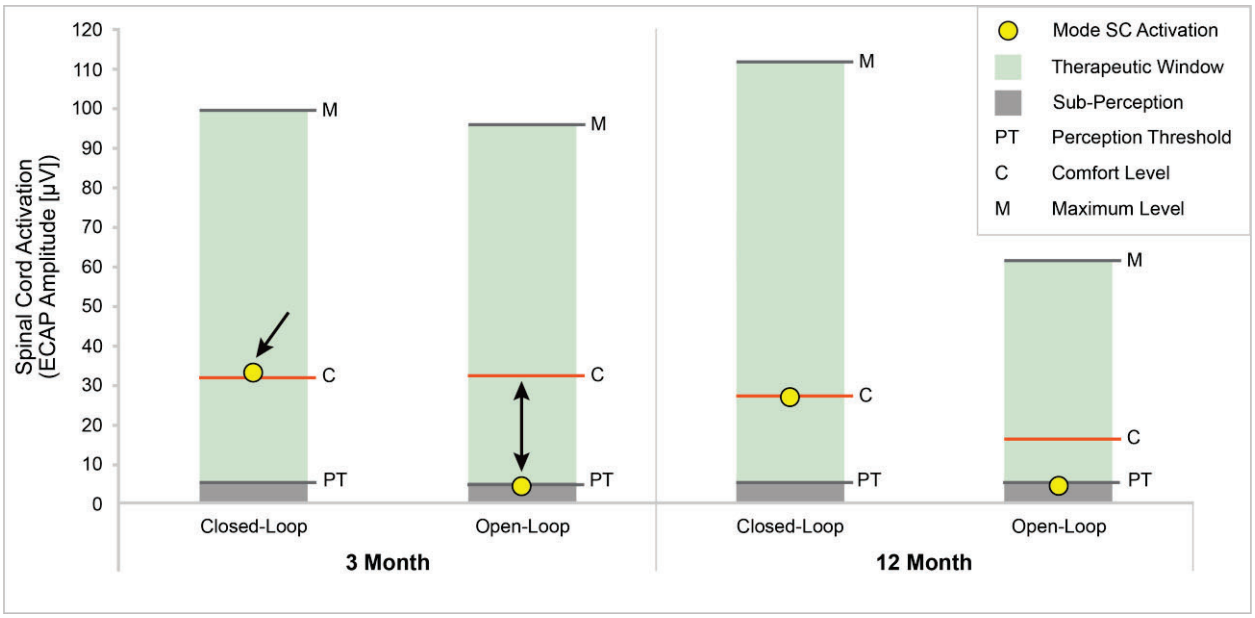
Because the Evoke System can measure the level of SC activation via ECAPs in both stimulation modes, the Evoke Study allowed for a direct comparison of SC activation between closed-loop (Investigational) and open-loop (Control) stimulation. The SC activation experienced by the subjects in both treatment groups was compared to their therapeutic range of activation (i.e., therapeutic window defined by the SC activation levels from patient perception threshold to maximum), as well as to the comfort level.

ECAP amplitudes at 3 months were similar for both groups for variables obtained in-clinic: therapeutic window width and comfort level. At 12 months, the width of the therapeutic window was decreased in the open-loop group compared to the closed-loop, as a result of changes in the maximum tolerable activation level. Additionally, whereas the ECAP amplitude for the comfort SC activation target level at 3 months was similar for both groups, at 12 months the open-loop group was decreased to about 60% of the level for the closed-loop group.

Outside the clinic, the most-frequent (mode) SC activation levels, indicating as-used amplitudes, were at least six times greater for closed-loop patients on average. The ratio of the mode to the comfort level was closer to 1 in the closed-loop group compared to the open-loop group, indicating, in general, closed-loop patients' most frequent SC activation level outside the clinic was closer to

their comfort level determined in the clinic. The proportion of time that patients' SC activation levels were within their therapeutic window was higher for the closed-loop group, with less time spent below and above the therapeutic window (Table II.19 and Figure II.6).

Clinically, these data demonstrate that, on average, the SC activation was maintained within the therapeutic window closer to the comfort level, a greater percentage of the time with closed-loop stimulation compared to open-loop stimulation. As seen in Figure II.6, on average, outside the clinic, the stimulation was turned down by patients in the open-loop group, with the most frequent SC activation level (yellow dot) reduced to patient perception threshold (PT), whereas it was maintained at the comfort level (C) in the closed-loop group.



Perception Threshold (PT): SC activation level the patient first feels a change in sensation (e.g., paresthesia, pain relief).
Comfort Level (C): SC activation level perceived as comfortable by the patient.
Maximum Level (M): maximum SC activation level the patient can withstand.
Therapeutic Window: SC activation levels from patient "perception threshold" to the "maximum level".
Mode SC Activation: most frequent SC activation level for a given period.

Figure II.6. Spinal Cord Activation Relative to the Therapeutic Window at 3 and 12 Months – ITT

Table II.19. Spinal Cord Activation Measurements at 3 and 12 Months – ITT

	3 Month		12 Month	
	Investigational	**Control**	**Investigational**	**Control**
Therapeutic Window (TW) (median)				
Perception Threshold to Maximum (Therapeutic Window (μV))	97.0	84.0	110.0	61.5
Perception Threshold (μV)	5.5	6.0	5.0	6.0
Comfort Level (μV)	31.5	32.0	27.0	16.0
Maximum (μV)	99.5	96.0	112.0	62.0
Percent Time in TW (%)	91.1	59.5	95.2	47.9
Percent Time Below Perception Threshold (%)	4.7	39.7	1.7	48.3
Percent Time Above Maximum (%)	0.0	0.7	0.0	0.3
ECAP Amplitude (μV) Histogram Characteristics (median)				
Mode	33.0	4.3	27.0	4.5
Mode/Comfort Level	0.8	0.1	0.9	0.4
(90th Percentile - 10th Percentile)/Median[1]	1.2	2.3	1.1	2.1

ECAP = Evoked Compound Action Potential; TW = Therapeutic Window
Kruskal-Wallis test between treatment groups.
[1] (90th Percentile – 10th Percentile)/Median is a measure of spread.

Subgroup Analyses

(1) High Responder Rate (≥80% VAS Pain Score Reduction)

The Evoke Study identified, a priori as a hierarchical secondary endpoint, a high responder threshold of ≥80% for VAS overall trunk and limb pain percent reduction as a way to evaluate high responders who achieved a particularly low level of pain following intervention. The results of that secondary endpoint, described above, demonstrated statistically comparable (i.e., non-inferior) results between groups at 3 and 12 months. Although statistical superiority was not demonstrated, there was a numerically greater percentage of subjects in the closed-loop group that experienced this level of pain relief compared to the control group. Given these results, a post-hoc analysis of the Evoke study data was conducted to evaluate the clinical meaningfulness of the high responder rate of ≥80% compared to the well-recognized substantial responder rate of ≥50% defined by IMMPACT. Pain relief as well as other domains considered important by chronic pain patients and the clinician/researcher recommended outcome domains identified by IMMPACT were compared between subjects with responder rates ≥50% and <80% (“responders”) versus ≥80% (“high responders”) at 3 and 12 months (4,5).

Refer to Table II.20 for a summary of the statistically significant differences (p-value < 0.05) in patient reported outcome (PRO) measures between responders and high responders (treatment groups combined). As seen in the table, on the PRO measures evaluated (ODI, POMS, and PSQI) at 3 and 12 months, the high responder group had statistically significantly greater improvements in mean scores from baseline and statistically significantly higher proportions of subjects with clinically meaningful changes, as applicable.

This post-hoc analysis is not without limitations. Since it was not pre-specified, the study was not powered to show a difference between these subgroups (i.e., subjects with VAS overall trunk and limb pain reduction ≥50% and <80% vs. ≥80%). However, the majority of the Evoke study ITT population at 3 (90/111 = 81.1%) and 12 months (90/103 = 87.4%) was included in this subgroup analysis. In addition, for all clinically relevant PROs evaluated, high responders showed statistically significantly better results for several of the summary measures supporting the robustness of the conclusions for this sub-analysis.

Table II.20. Differences in Patient Reported Outcomes between Responders and High Responders at 3 and 12 Months

	3 Months		12 Months	
Clinically Meaningful and Normal Population Comparisons	**VAS ≥50% and <80%**	**VAS ≥80%**	**VAS ≥50% and <80%**	**VAS ≥80%**
Oswestry Disability Index (ODI) Score				
ODI Mean (SD) Change from Baseline	23.5 (10.5)	36.4 (13.1)	22.9 (16.1)	31.3 (14.4)
ODI Percent Minimal Disability[1,2]	6/27 (22.2%)	41/63 (65.1%)	7/32 (21.9%)	28/58 (48.3%)
Profile of Mood States (POMS) Brief Total Mood Disturbance (TMD) Score[3]				
POMS TMD Mean (SD) Change from Baseline	9.7 (10.0)	20.5 (20.4)	10.3 (17.5)	20.9 (18.4)
POMS TMD Clinically Important Change from Baseline[4]	8/27 (29.6%)	37/63 (58.7%)	12/32 (37.5%)	35/58 (60.3%)
Pittsburgh Sleep Quality Index (PSQI) Score				
PSQI Mean (SD) Change from Baseline	3.7 (3.6)	6.2 (4.8)	4.4 (4.1)	6.4 (4.4)
PSQI Remission (Good Sleep Quality and Clinically Significant Change)[5]	2/27 (7.4%)	29/63 (46.0%)	4/32 (12.5%)	23/58 (39.7%)
PSQI Change from Baseline from Poor to Good Sleep Quality[6,7]	2/27 (7.4%)	29/61 (47.5%)	5/31 (16.1%)	23/57 (40.4%)
PSQI Change from Non-Normal at Baseline to Normal at Follow-up[7,8]	4/27 (14.8%)	32/61 (52.5%)	5/30 (16.7%)	26/57 (45.6%)

[1] Mapi Research Trust. Oswestry Disability Index Scoring Instructions.

[2] Evoke Study eligibility criteria required subjects have severe to crippled disability at baseline.

[3] POMS Brief normal values are not available.

[4] Dworkin, R. H. et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. J Pain 9, 105–121 (2008).

[5] Buysse, D. J. et al. Efficacy of brief behavioral treatment for chronic insomnia in older adults. Arch. Intern. Med. 171, 887–895 (2011).

6 Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R. & Kupfer, D. J. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28, 193–213 (1989).

[7] Does not include subjects who did not qualify for the Baseline condition or who did not have a follow-up.

[8] Buysse, D. J. et al. Relationships Between the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Clinical/Polysomnographic Measures in a Community Sample. J. Clin. Sleep. Med. 4, 563–71 (2008).

Two-sample t-test for continuous variables; Fisher's exact test for categorical variables. P-value < 0.05 indicated statistical significance.

Published Data

The Evoke System open-loop stimulation mode is equivalent to other commercially available SCS systems. Because the Evoke System was used in both arms of the pivotal clinical study, it is important to consider the results in the context of those reported in the published data for

similarly-designed devices. Table II.21 and Table II.22 display the safety and effectiveness outcomes for the Evoke System with the added context of the range of results reported for other commercially available systems. Such comparisons should be interpreted cautiously as study designs may impact results. For that reason, the publicly available information for other systems are provided as a range, rather than a direct comparison to results from specific studies. Table II.21 provides a comparison of the rates of study-related adverse events in the Evoke study to those for other commercially available SCS systems. As seen from this table, the type, rate, nature, and severity of adverse events in the Evoke study are consistent and comparable to these other systems. Table II.22 provides a comparison of effectiveness outcomes in the Evoke study to those for other commercially available SCS systems. As seen from this table, the effectiveness outcomes are comparable or better for the Investigational and Control groups in the Evoke study compared to these other systems.

Table II.21. Comparison of Safety of the Evoke System and Other Commercially Available SCS Systems

	Evoke Study N=134 Subjects		**Commercial SCS Systems**
Rates of Serious Study-Related Adverse Events			
Preferred Term	**Events n**	**Subjects n (%)**	**Subject Range[1-4] (%)**
Total Serious Adverse Events	**3**	**3 (2.2%)**	**0.0%-7.2%[1-4]**
Epidural Abscess	1	1 (0.7%)	0.0%-1.0%[4]
Lead Breakage/ Fracture	1	1 (0.7%)	NR
Wound Infection	1	1 (0.7%)	0.0%-2.0%[1,4]
Rates of Study-Related Adverse Events			
Preferred Term	**Events n**	**Subjects n (%)**	**Range[1-4]**
Total Adverse Events	**34**	**24 (17.9%)**	**17.9%-36.1%[1-4]**
Lead Migration	10	9 (6.7%)	1.3%-7.9%[1,2,4]
IPG Pocket Pain	5	5 (3.7%)	0.0%-9.9%[1,4]
Muscle Spasm or Muscle Cramp	3	3 (2.2%)	0.0%-2.6%[1,4]
Dural Puncture or Tear	2	2 (1.5%)	0.0%-3.8%[1,2,4]
IPG Malfunction due to Electrocautery	2	2 (1.5%)	1.3-3.8%[1,2]
Unwanted Stimulation Location	2	2 (1.5%)	4.0%[3]
Wound Infection	2	2 (1.5%)	0.0%-7.7%[1-4]
Dysesthesia - lower extremity	1	1 (0.7%)	0.0%-13.2%[1-4]
Epidural Abscess	1	1 (0.7%)	0.0%-1.0%[4]
Inadequate Lead Placement	1	1 (0.7%)	0.58%[3]
Lead Breakage/ Fracture	1	1 (0.7%)	NR
Low Back Pain	1	1 (0.7%)	0.0%-6.0%[1-3]
Nausea and/or vomiting	1	1 (0.7%)	NR
Skin Irritation or Redness	1	1 (0.7%)	0.0%-3.8%[1,2,4]
Wound Dehiscence	1	1 (0.7%)	0.0%-3.9%[1,4]

[1]Medtronic Clinical Summary (2014-10), RestoreSensor SCS System 6-week cross-over study results (PMA Number: P840001) (10)
[2]Boston Scientific (formerly Advanced Bionics) Precision SCS System SSED, Precision SCS System study results through 6 months (PMA Number: P030017) (11)

	Evoke Study N=134 Subjects	Commercial SCS Systems
[3]Abbott (formerly St. Jude Medical) Proclaim SCS System Clinician's Manual (2018-02), SUNBURST 12-week crossover study results (PMA Number: P010032) (12) [4]Nevro Senza SCS System SSED, Senza 12-month parallel arm study results (PMA Number: P130022) (13)		

Table II.22. Comparison of Effectiveness Outcomes of the Evoke System and Other Commercially Available SCS Systems

	Through 3-Month Follow-up			Through 12-Month Follow-up		
	EVOKE STUDY[1]			EVOKE STUDY[5]		
Outcome Measure	Investigational	Control	Commercial SCS Systems – Range[2-4]	Investigational	Control	Commercial SCS Systems – Range [6]
VAS Overall Pain – Raw Score	22.1	33.1	41.4 - 46.3[2,3]	23.4	35.5	NA
VAS Overall Pain – Change from Baseline	59.8	49.2	14.8 - 32.1[2,3]	58.1	46.4	NA
VAS Overall Pain – ≥30% Reduction	88.7%	69.8%	51.0% - 60.0%[3]	86.4%	64.4%	NA
VAS Overall Pain – ≥50% Reduction	82.3%	60.3%	32.0% - 39.0%[3]	83.1%	61.0%	NA
VAS Back Pain – Raw Score	23.3	33.8	27 - 48[3,4]	25.3	36.8	33 - 50[6]
VAS Back Pain – Change from Baseline	58.2	46.6	31 - 49[4]	55.7	43.3	31 - 47[6]
VAS Back Pain – Percent Reduction	72.1%	57.5%	38.4% - 62.8%[4]	69.4%	54.0%	40.3% - 62.7%[6]
VAS Back Pain – ≥50% Reduction	80.6%	57.1%	39.1% - 78.3%[4]	79.7%	57.6%	46.0% - 73.9%[6]
VAS Leg Pain – Raw Score	19.5	25.8	25 - 41.6[3,4]	22.7	30.4	31 - 49[6]
VAS Leg Pain – Change from Baseline	62.7	54.2	37 - 49[4]	59.3	49.1	33 – 47[6]
VAS Leg Pain – Percent Reduction	76.8%	67.8%	44.1% - 64.9%[4]	72.9%	62.1%	42.4% - 65.4%[6]
VAS Leg Pain – ≥50% Reduction	80.6%	68.3%	48.3% - 77.2%[4]	83.1%	61.0%	43.7% - 75.0%[6]
ODI – Raw Score	24.4	29.3	35.5 - 35.6[3]	26.7	29.9	NA
ODI – Percent Change from Baseline	55.3%	48.7%	24.9% - 32.2%[4]	50.9%	47.6%	21.6% - 29.2%[6]
ODI – Percent Minimal to Moderate Disability	84.5%	77.4%	47.1% - 64.1%[4]	80.0%	70.8%	40.2% - 58.7%[6]
SF-12 PCS – Change from Baseline	13.9	11.5	6.1 - 9.4[4]	11.7	11.6	6.0 – 8.1[6]
SF-12 MCS – Change from Baseline	8.9	1.9	1.6 - 2.0[4]	7.4	-0.8	1.2 – 2.6[6]
PSQI – Change from Baseline	5.7	4.5	2.1 - 3.1[4]	5.7	4.5	1.8 – 2.6[6]

Outcome Measure	Through 3-Month Follow-up			Through 12-Month Follow-up		
	EVOKE STUDY[1]		Commercial SCS Systems – Range[2-4]	EVOKE STUDY[5]		Commercial SCS Systems – Range [6]
	Investigational	Control		Investigational	Control	
PGIC – Very Much, Much, or Minimally Improved	98.3%	94.3%	74.0% - 74.2%[3]	100.0%	95.8%	NA
PGIC – Very Much or Much Improved	89.7%	81.1%	36.7% - 52.2%[4]	81.8%	75.0%	33.8% - 52.8%[6]
Subject Satisfaction – Very Satisfied or Satisfied	94.8%	86.8%	78.1%[3]	90.9%	85.4%	NA
Subject Satisfaction – Very Satisfied	74.1%	58.5%	33.8% - 54.1%[4]	65.5%	64.6%	32.3% - 55.4%[6]

[1]Evoke Study 3-month parallel arm study results.
[2]Medtronic Clinical Summary (2014-10), RestoreSensor SCS System 6-week cross-over study results (PMA Number: P840001) (16)
[3]Abbott (formerly St. Jude Medical) Proclaim SCS System Clinician's Manual (2018-02), SUNBURST 12-week crossover study results (PMA Number: P010032) (18)
[4]Nevro Senza SCS System SSED, Senza 3-month parallel arm study results (PMA Number: P130022) (13)
[5]Evoke Study 12-month parallel arm study results.
[6]Nevro Senza SCS System SSED, Senza 12-month parallel arm study results (PMA Number: P130022) (13)

II.B. Summary of Supplemental Clinical Information

1. Long-term Study Results from an Australian Prospective Study of the Evoke System (Avalon Study)

The Avalon study (ANZCTR Identifier: ACTRN12615000713594) is a prospective, multicenter, single-arm study designed to assess the safety and performance of the Saluda Medical Evoke System closed-loop stimulation for the treatment of chronic, intractable pain of the trunk and/or limbs. This study was approved by each of the four participating centers' ethics committees and performed in accordance with ISO 14155, Declaration of Helsinki, International Conference of Harmonisation (ICH) GCP, and Therapeutic Goods Administration (TGA) applicable regulations and/or guidelines. Subjects who provided informed consent and met the study eligibility criteria underwent a trial with the external trial stimulator to determine if the subject was eligible for the permanent implant. Subjects who had at least a 40% reduction in pain compared to baseline as measured by VAS were approved to receive a permanent implant of the Evoke SCS System. Subjects were followed up at 1-, 3-, 6-, and 12-months following the permanent implant, and quarterly thereafter through 24-months if subjects consented to extended follow-up.

The baseline demographics and characteristics of the Avalon study population were similar to those for the Evoke study population. The mean age of subjects enrolled in the Avalon study was 56.3 years and 50% of subjects were male. The mean body mass index (BMI) at baseline was 30.3 kg/m^2. The mean duration of chronic pain for enrolled subjects was 14.3 years. The predominate primary diagnosis of enrolled subjects was Failed Back Surgery Syndrome/Failed Neck Surgery Syndrome (FBSS/FNSS) (Note: none of the subjects' primary area of pain was the neck or upper extremities), followed by radiculopathy.

Subject enrollment, the primary endpoint analysis, and 24-month follow-up are complete. The first subject was enrolled (i.e., had a trial procedure) in the Avalon study on August 25, 2015 and the first permanent implant occurred on October 13, 2015. There were 70 trial procedures and 50 permanent implant procedures. On average, subjects had a permanent implant for 21.0 months (range, 0.5 to 25.8 months). The cumulative implant months of experience for the subjects that received a permanent implant was 1052.3 months (87.6 years). Of the 50 subjects who received the permanent implant, 49 completed the 1 Month visit, 45 the 3 Month visit, 46 the 6 Month visit, 43 the 12 Month visit, 37 the 15 Month visit, 39 the 18 Month visit, 38 the 21 Month visit, and 38 the 24 Month visit.

This study demonstrated sustained high rates of VAS overall pain reduction through 24 months, with percent reduction from baseline ranging from 71.2% to 81.2%, responder rates (≥50% reduction) ranging from 78.3% to 89.5%, and high responder rates (≥80% reduction) ranging from 42.2% to 69.2% throughout follow-up (Table II.23).

The type, rate, nature, and severity of adverse events that have occurred in the Avalon study were consistent and comparable to the Evoke study and to reported adverse events in the literature and from available market data for other SCS systems.

Table II.23. Avalon Study VAS Overall Pain Reduction through 24 Months

Overall Pain	3 Month	6 Month	12 Month	15 Month	18 Month	21 Month	24 Month
Number of subjects	45	46	43	37	39	38	38
Mean (SD) Percent Reduction from Baseline	71.2 (27.0)	71.7 (30.5)	73.6 (28.0)	76.3 (28. 5)	79.7 (23.1)	77.5 (27.1)	81.2 (24.0)
95% CI	(63.0-79.3)	(62.6-80.8)	(65.0-82.2)	(66.8-85.8)	(72.2-87.2)	(68.6-86.4)	(73.3-89.1)
Responders (≥50% reduction)	80.0%	78.3%	81.4%	81.1%	84.6%	81.6%	89.5%
High Responders (≥80% reduction)	42.2%	52.2%	53.5%	64.9%	69.2%	68.4%	68.4%

II.C. Conclusions Drawn from Preclinical and Clinical Studies

1. Effectiveness Conclusions

Effectiveness for the Evoke System was based on a double-blind, randomized, controlled, pivotal study (Evoke study) comparing ECAP-controlled, closed-loop SCS to open-loop SCS. The Evoke System is capable of operating either in the open-loop stimulation mode (equivalent to other commercially available SCS systems) or in the closed-loop stimulation mode. The device includes the ability to measure ECAP amplitude (SC activation) in both stimulation modes. Thus, the Evoke System was used in both study groups, facilitating a direct comparison of closed-loop stimulation to open-loop stimulation.

One-hundred and thirty-four (134) subjects were enrolled and randomized (67 in the Investigational [closed-loop] group and 67 in the Control [open-loop] group). Baseline assessments demonstrated treatment groups were well-matched with no statistical differences in demographic and baseline characteristics. Of the 134 subjects randomized, 125 subjects (62 Investigational subjects, 63 Control subjects) had known endpoint status or were classified as a presumed non-responder and were included in the ITT population at 3 months. At 12 months, 118 subjects (59 Investigational subjects, 59 Control subjects) had known endpoint status or were classified as a presumed non-responder and were included in the ITT population.

The results of the primary composite endpoint, which evaluated pain relief in combination with no increase in baseline pain medication, successfully demonstrated both non-inferiority (p-value < 0.001) and superiority(3 months: p-value = 0.005; 12 months: p-value = 0.006) of ECAP-controlled, closed-loop stimulation to open-loop stimulation. In total, greater than 82% (3 months: 82.3%; 12 months: 83.1%) of Investigational subjects met the primary endpoint individual success criteria compared to approximately 60% (3 months: 60.3%, 12 months: 61.0%) of Control subjects. Additionally, the analysis of the primary endpoint was performed in the PIS population, the subset of subjects in the ITT population with a permanent implant, and demonstrated both non-inferiority (p-value < 0.001) and superiority (3 months: p-value = 0.031; 12 months: p-value = 0.039) of closed-loop stimulation (3 months: 87.9%; 12 months: 89.1%) to open-loop stimulation (3 months: 71.7%; 12 months: 73.5%), confirming the robustness of the study conclusions. Thus, regardless of the methodology used to analyze the primary endpoint, the results consistently demonstrated superiority in clinical outcomes associated with closed-loop stimulation compared to open-loop stimulation.

Non-inferiority was demonstrated across all of the hierarchical secondary endpoints (p-values ≤ 0.002). In addition, numerically better improvement was consistently observed, with statistical superiority of closed-loop stimulation to open-loop stimulation in the percentage change in VAS average back pain at 3 months (72.1% Investigational vs. 57.5% Control, p-value = 0.045) and incidence of ≥50% reduction in VAS average back pain at 3 and 12 months (3 months: 80.6% Investigational vs. 57.1% Control, p-value = 0.013; 12 months: 79.7% Investigational vs. 57.6% Control, p-value = 0.032).

Analysis was also conducted to evaluate the extent of SC activation during treatment in the two study groups. This analysis helps to assess the mechanism of action of SCS, providing the clinical explanation for the results observed in the primary and secondary study endpoints. That analysis showed statistically significant differences in spinal cord activation for closed-loop compared to open-loop SCS. The difference in the predefined endpoints between the closed-loop SCS and open-loop SCS appears to be due to the activation of the spinal cord, which can be explained by inhibition of the dorsal horn through modulation of the activity by dorsal column Aβ sensory fibers.

Additionally, long-term effectiveness has been demonstrated with the Evoke System in the Avalon study with VAS overall pain reduction ranging from 71.2% to 81.2%, responder rates (≥50% reduction) ranging from 78.3% to 89.5%, and high responder rates (≥80% reduction) ranging from 42.2% to 69.2% from 3 months to 24 months post-implant.

The results of the clinical studies demonstrate a clinically meaningful reduction in pain with the Evoke System for patients who suffer from chronic, intractable pain of the trunk and/or limbs. In addition, the available data successfully demonstrate that use of closed-loop therapy provides a

meaningful clinical benefit and advantage compared to use of open-loop therapy. Given that currently available systems offer only open-loop therapy, the availability of the Evoke System provides an important clinical benefit.

2. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies, as well as data collected in clinical studies conducted to support PMA approval as described above. The risks of the device were also compared to those for other similar commercially available SCS systems.

The type, nature, and severity of adverse events in the clinical studies of the Evoke System were consistent with the published data for other commercially available SCS systems. There have been no UADEs (Evoke study) or USADEs (Avalon study). The study-related adverse events that have been reported are known risks, and the severity and rate are not outside what is expected for SCS systems.

Among the 134 randomized subjects in the Evoke study, a total of 254 adverse events (AEs) in 90 subjects (67.2%) were reported (150 AEs, 67.2% Investigational subjects; 104 AEs, 67.2% Control subjects). 13.4% of all adverse events were study-related, with 3.1% being related to the stimulation therapy. There were no differences between groups in study-related (device, procedure and/or stimulation therapy) adverse events, or stimulation therapy-related adverse events specifically.

A total of 27 serious adverse events (SAEs) in 18 subjects (13.4%) were reported (16 SAEs, 14.9% Investigational subjects; 11 SAEs, 11.9% Control subjects). None of the serious adverse events were classified as stimulation-related in either treatment group. There were three study-related serious adverse events in three subjects (1 Investigational and 2 Control) (2.2%) including wound infection, epidural abscess, and lead breakage/fracture. These are known risks, and the severity and rate are not outside what is expected for SCS systems.

Additionally, long-term safety has been demonstrated with the Evoke System in the Avalon study with follow-up out to 24 months. The type, rate, nature, and severity of adverse events that have occurred in the Avalon study were consistent and comparable to the Evoke study and to reported adverse events in the literature and from available market data for other SCS systems.

In the Evoke study, measurement of ECAPs was recorded successfully in all Investigational and Control subjects (N=103) and enablement of closed-loop was effective in all Investigational subjects (N=55) at 12 months. In addition, all subjects in the Avalon study who completed the 24-month visit (38 patients) were able to have their stimulator successfully programmed to measure ECAPs and stimulate with closed-loop enabled. There have been no reports of adverse events or discontinued stimulator use due to degradation of ECAP recordings.

3. Benefit-Risk Conclusions

The probable benefits and risks of the device are based on data collected in the clinical studies conducted to support PMA approval as described above.

Chronic pain is defined as pain that lasts more than three to six months beyond the normal time of healing (14). It results in significant morbidity with tremendous physical, mental, emotional, and financial burden to the individual persons, their families, and society as a whole.

Chronic pain is treated on a continuum, as mentioned above, with first line treatments including conservative care (e.g., physical therapy, acupuncture, biofeedback, non-opioid pain medications), second line treatments that are more intensive (e.g., systemic opioids, injections, nerve blocks), and last line treatments including surgical intervention (e.g., implantable SCS systems, intrathecal drug delivery (IDD) systems, surgical repair of anatomical issues, or surgical techniques to destroy nerve pathways). The risk profile for SCS therapy has advantages compared to reconstructive surgeries and neuroablation due to the fact it is reversible as the device can be surgically removed. Furthermore, typically patients undergo a trial period with SCS, in which leads are temporarily placed in the epidural space and connected to an external trial stimulator, to assess tolerability (e.g., of the stimulation sensation and the device) and the degree of pain relief prior to being permanently implanted. In addition, SCS therapy has the advantage of not having drug side effects, including respiratory distress associated with IDD systems, and addictive properties and potential for overdose associated with opioid usage, which is currently of epidemic proportions in the US.

The Evoke SCS system is novel in that it is the first SCS system to have the ability to continuously measure in vivo human spinal cord activation in real-time during daily use. In addition to using this information to produce closed-loop stimulation to maintain consistent activation for this therapy, measurement of ECAPs can be used to confirm therapy is being received and to optimize programming (for both open-loop and closed-loop stimulation modes). As seen by the substantial improvements in outcomes in the Control group in the Evoke study, objective measurement of ECAPs during programming, in and of itself, may contribute to improved outcomes. Moreover, ECAP measurement may be used to gain insight into the mechanism of action of SCS and the condition of the spinal cord, as well as monitor the health of the spinal cord and the effects of treatment over time. This may be extended to other treatments that effect neural activation such as some types of pain medications (e.g., anticonvulsants and opioids), where measurement of ECAPs may be used to titrate and optimize dosing, as well as measure the interaction between these medications and SCS.

The benefit of the Evoke System was demonstrated in the Evoke study. High rates of substantial improvement (i.e., ≥50% reduction in back and leg pain (15)) with no increase in pain medications were observed in both closed- and open-loop stimulation using ECAP measurements to optimize therapy. Greater improvement of closed-loop compared to open-loop SCS was demonstrated by the robustness of the primary and hierarchical secondary endpoint outcomes. The primary endpoint and all hierarchical secondary endpoints successfully demonstrated non-inferiority. Additionally, closed-loop stimulation was statistically superior to open-loop stimulation with respect to the rate of at least 50% reduction in overall back and leg pain (primary endpoint; approximately 80% vs. 60%, respectively) and in back pain specifically (hierarchical secondary endpoint; approximately 80% vs. 57%, respectively). Additionally, the Avalon study has demonstrated sustained long-term rates of substantial improvement (i.e., ≥50% reduction) in VAS overall pain relief (≥78% of subjects) with the Evoke System. It would be expected that patients with chronic pain would experience a similar benefit.

Patient perspectives were also considered during the review and included patient satisfaction with the therapy and global impression of change in the Evoke study. Greater than 90% of Investigational subjects and greater than 80% of Control subjects were very satisfied or satisfied with their therapy (3 Months: 94.8% Investigational, 86.8% Control; 12 Months: 90.9% Investigational, 85.4% Control). Additionally, approximately 90% of Investigational subjects and 80% of Control subjects at 3 months (89.7% Investigational, 81.1% Control), and approximately 80% of Investigational subjects and 75% of Control subjects at 12 months (81.8% Investigational, 75.0% Control), indicated their overall status was very much or much improved, reflecting clinically important improvement.

As described above, the Evoke System was determined to be safe. The adverse events that were reported in both the Evoke and Avalon studies were consistent with the well-known safety profile of other similar commercially available SCS systems as reported in the published data.

Additional factors related to the Evoke study to be considered in determining probable risks and benefits for the Evoke System include study design and execution. The randomized, double-blind study design was developed to preserve objectivity and minimize unintentional bias. The randomization in this study produced well matched treatment groups with respect to baseline characteristics as well as neurophysiological properties, supporting the validity of the comparisons between groups. Subjects in both treatment groups received equal care, with the device, implant procedure, and programming (i.e., frequency of visits, duration of visits, and programming parameters) being the same for both groups. Programming in both groups utilized ECAP measurement in addition to subject feedback to optimize patient outcomes. As recommended by the FDA, Investigator oversight of the Field Clinical Engineers (FCEs) was documented to confirm comprehensive programming and optimization for all study subjects (16). Additionally, none of the subjects or Investigators were unblinded to the treatment assignment, reducing the potential of data being systematically distorted by knowledge of the treatment received.

In conclusion, the overall safety profile of the Evoke System appears to be very similar to that of other commercially available SCS options, while closed-loop stimulation demonstrated clinically meaningful advantage and superior outcomes compared with the type of open-loop therapy available from other commercial systems. Thus, the clinical benefits of the Evoke System clearly outweigh any associated risks.

4. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the Evoke System when used in accordance with the indications for use in both open-loop and closed-loop mode. The results from the clinical studies support a reasonable assurance of the safety and efficacy of the Evoke System, as well as its long-term performance, when used in a manner consistent with its labeling and intended use. The evidence supporting the safety and effectiveness of the Evoke System is based on a non-inferiority/superiority pivotal study, a long-term prospective study, and over 30 years of clinical research and experience documented in the published data on fully implantable SCS systems and the similarities of the Evoke System to commercially available implantable SCS systems. The results from comprehensive pre-clinical testing show that the Evoke System performs as intended. The analyses also support a clinical benefit to risk determination that is favorable.

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III. DIABETIC PERIPHERAL NEUROPATHY

The Evoke System was subsequently approved to expand the indication to include painful diabetic peripheral neuropathy (DPN) of the lower extremities:

> *The Saluda Medical Evoke SCS System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following:*
>
> - *Failed back surgery syndrome*
> - *Intractable low back pain and leg pain*
> - *Diabetic peripheral neuropathy of the lower extremities*

The summary of primary clinical studies supporting the expanded indication of DPN for the Evoke System is summarized in section III.A below.

III.A. Summary of Primary Clinical Studies

The Evoke System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain. The safety and effectiveness of the Evoke System has been previously established for the approved indications (see section II).

The clinical evidence supporting the safe and effective use of the Evoke System in the diabetic neuropathy population is based on a systematic review of published clinical scientific literature of commercially available SCS systems. Primary evidence comes from two randomized controlled trials in patients with diabetic peripheral neuropathy (DPN). Additional supplemental clinical evidence for safety was identified through the analysis of Evoke System clinical study safety data, investigating adverse event data related to the use of the Evoke System in patients with diabetes.

1. Study Design

The safety and effectiveness of the Evoke System to treat DPN was based primarily on a systematic review of published scientific literature reporting on the use of commercially available spinal cord stimulation (SCS) systems for the treatment of chronic intractable pain in a diabetic population. A systematic review of published literature was conducted by searching the Embase and PubMed databases for terms relating to SCS and diabetes. As a supplemental body of evidence to support safety, Saluda Medical also analyzed clinical study safety data from patients implanted with the Evoke System. Finally, a systematic search of the published literature was conducted to identify recent guidelines on perioperative care of diabetic patients to inform the labeling.

Safety

The safety objective is to identify risks relevant to SCS to which diabetic patients are predisposed and to characterize the safety profile of SCS to treat DPN.

The safety profile of the Evoke System to treat DPN was characterized through analysis of published scientific literature and clinical study safety data from patients implanted with the Evoke System. The analysis characterized the overall safety profile by common adverse events, as well as

specifically examining the risks to which the diabetic population are pre-disposed such as inherent surgical complications that may occur more frequently or have greater impact in these patients. Publications reflecting the experience of patients treated with SCS for DPN and patients treated with SCS for any condition where a diagnosis of diabetes was considered were included. Publications reporting on studies where adverse events were reported in a comprehensive manner were pooled with the clinical study safety data of the Evoke System to create an overall safety profile.

Effectiveness

The effectiveness objective is to characterize the clinical benefits related to pain relief for SCS used to treat DPN when compared to the standard-of-care.

The effectiveness of the Evoke System to treat DPN was demonstrated through analysis of clinical study results identified from the systematic review of published scientific literature. Effectiveness was demonstrated by the probability of treatment success. The probability of treatment success (i.e., Responder Rate or proportion of successfully treated subjects) was defined by a specified percent reduction in pain rating or Patient Global Impression of Change (PGIC) rating and the magnitude of pain relief as measured through reduction in pain scores from a Numeric Rating Scale (NRS) or Visual Analog Scale (VAS).

Additionally, all publications reporting on the non-comparative studies (i.e., prospective single-arm studies) were included and summarized.

2. Evoke System Clinical Study Safety Data

Two Investigational Device Exemption (IDE) studies have been conducted evaluating the Evoke System to treat patients with chronic trunk and/or limb pain. The Evoke Study (NCT02924129), which is complete with 134 enrolled subjects, was a multicenter, double-blind, randomized controlled trial (RCT) with 36-month follow-up. The ECAP study (NCT04319887), which is ongoing with 300 enrolled subjects, is a prospective, multicenter, single-arm study with 24-month follow-up. The safety data for subjects enrolled in these studies who had diabetes were evaluated.

Data Selection

Patients enrolled in the Evoke and ECAP studies were categorized into two cohorts: 1) Diabetes: patients with diabetes, and 2) non-Diabetes: patients without diabetes. The incidence of related adverse events up to 36 months following implantation were compared between the two cohorts to determine whether patients with diabetes who are implanted with SCS exhibited an increased risk of related adverse events when compared to the general population of SCS patients. For both cohorts, the incidence of subsequent surgical interventions (i.e., device revision, replacement, or explant) following implantation were also evaluated.

3. Literature Search Strategy

The databases searched include Embase and PubMed. The databases were searched to ensure comprehensive coverage of globally published clinical evidence for medical device products and therapies.

Two separate systematic searches and reviews were conducted. For both searches, the publications identified from databases were assessed for inclusion in the review through two steps. First, two reviewers independently screened initial search results for the selection criteria. Next, full-text copies of the selected publications were assessed independently by the same two reviewers for inclusion as final selections. Differences in selection between the two reviewers were discussed to confirm selection or rejection. A third party was not necessary to resolve disputed selections.

1. Safety and effectiveness of SCS to treat DPN
    a. Search terms (including expanded terms): Diabetes AND spinal cord stimulation or dorsal column stimulation
    b. Search dates: 1984-2023
    c. Selection criteria:
        i. Safety: Publication must include data on a distinctly identifiable diabetic population and report comprehensive detail on adverse events or an analysis of the impact of a diabetic state on a safety-related outcome.
        ii. Effectiveness: Publication must include data from studies on SCS to treat DPN with quantifiable information regarding pain reduction, probability of treatment success, or quality of life improvements. Any available meta-analyses were included if the report synthesized new data based on prospective studies.
2. Clinical practice guidelines on perioperative care of diabetic patients
    a. Search terms (including expanded terms): Diabetes AND Clinical practice guideline or consensus statement AND peri-, post-, pre- operative or surgical
    b. Search dates: 2017-2023
    c. Selection criteria: The guideline must provide specific recommendations for steps to be taken to avoid complications of surgery in a diabetic population. The publication must include a comprehensive list of specific steps, which are generalizable to SCS procedures.

Results of search and screening

(1) Clinical practice guidelines for perioperative care of diabetic patients

Initial screening was performed on 233 titles and abstracts resulting in the selection of 57 publications for full-text review. After full-text review, 30 publications were selected for inclusion. Guidelines are summarized in Table III.1.

Table III.1. Selected Guidelines

Author and Title	Summary	Recommendations	Noted Complications
American Diabetes Association Professional Practice Committee. 16. Diabetes Care 2022 (1) Diabetes care in the hospital: Standards of Medical Care in Diabetes—2022.	Article from the American Diabetes Association provides guidelines for the care of diabetic patients in the hospital. Article includes a specific section on the care of perioperative patients.	• The target range for blood glucose in the perioperative period should be 80–180 mg/dL (4.4–10.0 mmol/L). • A preoperative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease and those with autonomic neuropathy or renal failure. • Metformin should be withheld on the day of surgery. • SGLT2 inhibitors must be discontinued 3–4 days before surgery. • Withhold any other oral glucose lowering agents the morning of surgery or procedure and give half of NPH dose or 75–80% doses of long-acting analog or pump basal insulin. • Monitor blood glucose at least every 2–4 hours while the patient is taking nothing by mouth and dose with short- or rapid- acting insulin as needed.	• "perioperative complications", no specifics provided
Arthur et al. Braz J Cardiovasc Surg. 2018 (2) Perioperative Management of the Diabetic Patient Referred to Cardiac Surgery	Presents recommendations for perioperative management of hyperglycemia in patients (with or without diabetes) undergoing cardiovascular surgery.	• All diabetic patients should receive continuous insulin infusion during surgery and for at least 24 hours postoperatively to maintain blood glucose levels < 180 mg/dL. • Intravenous insulin therapy is preferred due to rapid titration. • Continuous insulin infusion should be used instead of subcutaneous injections or intermittent intravenous insulin bolus. • Diabetic patients receiving continuous insulin should maintain it until after dinner the night before surrey. • All hypoglycemic agents and non-insulin oral diabetes medications should be maintained up to 24 hours before surgery. • Level of glycated HbA1c should be assessed prior to surgery. Adequate glycemic control is associated with HbcA1c < 7%. • Before surgery, blood glucose level should be below 180 mg/dL. • Patients with or without diabetes and persistently elevated blood glucose levels (> 180 mg/dL) should receive intravenous insulin infusions to maintain blood glucose levels ≤ 180 mg/dL during their stay in ICU.	• Neurological events • Neurobehavioral deficits, and neurological-related deaths • All-cause mortality, myocardial infarction, acute heart failure • Recurring angina, wound infection

Author and Title	Summary	Recommendations	Noted Complications
		• Patients requiring ≥ 3 days in ICU due to ventilator dependence or the need for inotropes, continuous venovenous hemodialysis or hemofiltration, and antiarrhythmic intra-aortic balloon or left ventricular assist device should receive continuous infusion of intravenous insulin to maintain a blood glucose level < 150 mg/dL, regardless of whether or not they are diabetics. • Oral antidiabetics should be restarted in patients with adequate blood glucose levels, with few exceptions.	
Berhe et al. Intl. J. Surg. 2017 (3) Guideline on perioperative glycemic control for patients with diabetic mellitus: Resource limited areas.	Review and guideline of diabetic patients undergoing surgery, differentiated by minor or major surgery, aimed at resource limited health systems	• Urinalysis and electrolyte test results should be available at pre-operative screening. • Prioritize operation for first of the day. • Fast before surgery, unless procedure later in day, then light meal with half dose of fast acting insulin. • When fasting, check glucose every 2 hours, and 1 hour prior to surgery. • Target range for blood glucose: ○ 108-180 mg/dL and 72-216 mg/dL is acceptable ○ Postpone elective surgery if over 300 mg/dL or HbA1c > 69 mmol/L, and consult specialist for management	• Post-operative infection • Surgery stress causing diabetic ketoacidosis • Hyperglycemia • Hyperosmolar state • Increased morbidity and mortality • Hypoglycemia leading to somnolence, confusion, seizures, irreversible neurological injuries • Impaired wound healing • Increased occurrence in cardiac arrythmias
Bhattacharya et al. World J Diabetes. 202 (4) Expert opinion on the preoperative medical optimization of adults with diabetes undergoing metabolic surgery	Provides recommendations on perioperative medical management for individuals with diabetes mellitus who are undergoing metabolic surgery.	• Initial preoperative assessment should include a comprehensive medical, psychosocial and drug history, along with physical examination. • Tests for FPG (fasting plasma glucose), postprandial glucose and HbA1c should be included in laboratory workup. • A glycemic target of HbA1c <7% before surgery is a reasonable goal. • Medical nutrition therapy, physical exercise, and pharmacotherapy should be optimally integrated to attain that goal. Pharmacological agents known to induce weight loss, such as sodium-glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, should be considered as part of the treatment armamentarium whenever	• Postoperative hyperglycemia • Wound Infection • Acute renal failure

Author and Title	Summary	Recommendations	Noted Complications
		feasible. Drugs known to cause weight gain, such as sulfonylureas and thiazolidinediones, should be avoided as long-term therapeutic strategy if possible. The perioperative risks of deranged glycemic control vs benefits of early metabolic surgery have to be assessed on a case-to-case basis if glycemic control cannot be attained preoperatively despite optimal medical treatment. If a strategy of restricting calories with meal replacement therapy is employed in the preoperative weeks, the anti-diabetic medications would need to be reduced to prevent hypoglycemia. • After admission, most non-insulin based therapies should be stopped, and the patient should be transitioned to insulin as per institutional practice. Severe degrees of hyperglycemia will require intravenous insulin infusion. Target glucose of 100 to 180 mg/dL (5.5-10 mmol/L) is acceptable in the perioperative period.	
Chan et al. Anaesth. Intensive Care Med. 2020 (5) Preoperative cardiac optimization	Guideline for peri-operative cardiac optimization, considering diabetes among other comorbidities	• Peri-operative target for blood glucose of 6-10 mmol/L. • Glycemic control should be checked at the time of surgery. • Diabetic patients should be identified early in pre-operative pathway. • Tests for comorbidities should be conducted including electroconvulsive therapy (ECT), urea and electrolytes for all patients. • Surgery should be scheduled early in the day to avoid disruption of glycemic control.	Autonomic neuropathy can cause perioperative hemodynamic instability
Cheisson et al. Anaesthesia, critical care & pain medicine. 2018 (6) Perioperative management of adult diabetic patients – Intraoperative Period	Practice guideline focusing on the intra-operative management of diabetic patients from the French Society of Anaesthesia and Intensive Care and the French society for the Study of Diabetes	• Avoid prolonged fasting by scheduling procedures early in the day. • Have a blood glucose goal of 5-10 mmol/L, avoiding hypoglycemia. • If insulin is required, use fast acting analog subcutaneously with electronic syringe with IV glucose. • Replace insulin pump with immediate IV management during procedure. • Monitor glucose every 1-2 hours and potassium every 4 hours if under insulin control, and consider 3.8 mmol/L hypoglycemia requiring intervention.	• Infections • Delayed wound healing • Increased morbidity and mortality

Author and Title	Summary	Recommendations	Noted Complications
		• All solutes may be used, including Ringer's lactate, in the peri-operative period. • Peri-operative control is dictated by 3 factors: diabetes type, pre-operative control, and type of surgery. • Manage risk of nausea and vomiting to facilitate resumption of food intake after surgery. • Manage post-operative pain closely to avoid hyperglycemia.	
Cheisson et al. Anaesthesia Critical Care & Pain Medicine. 2018 (7) Perioperative management of adult diabetic patients. Postoperative period.	Practice guideline focusing on the post-operative management of diabetic patients from the French Society of Anaesthesia and Intensive Care and the French Society for the Study of Diabetes	• Maintain subcutaneous insulin via electronic syringe until glucose stabilizes (<10 mmol/L) and discontinue when normal feeding resumes. • Manage discontinuation with appropriate slow and fast acting insulins. • Resume treatments based on diabetes type, management regimen and post-operative glucose levels.	Hyperglycemia (ketoacidosis) and Hypoglycemia
Cornelius et al. Anesth Prog. 2017 (8) Patients With Type 2 Diabetes: Anesthetic Management in the Ambulatory Setting: Part 2: Pharmacology and Guidelines for Perioperative Management	An analysis of diabetic medication pharmacology and guidelines for blood glucose management in an ambulatory surgery setting.	• Antidiabetic drugs should not be taken on the day of surgery, but should not be discontinued the day prior to surgery. • Metformin may be discontinued 24-48 hours prior to surgery in patients with renal insufficiency. • Post-surgical medication regimens only should be restarted after normal food intake resumes. • Short-acting or rapid-acting insulin therapy should be withheld on the morning of surgery. • Long and intermediate acting insulin should be taken at 75-100% and 75% respectively the evening prior to the surgery day. Mixed/intermediate insulin doses should be taken in the morning at 50% of usual dose. • In the anesthetized diabetic patient, 70 mg/dL (3.9 mmol/L) of blood glucose is the trigger level for treatment for hypoglycemia. • Hypoglycemia is managed in conscious patients through diet + gel/glucose tablets. Unconscious patients can receive intravenous administration of dextrose.	• Postoperative nausea and vomiting • Compromised wound healing • Postoperative glycemic stability

Author and Title	Summary	Recommendations	Noted Complications
		• Hyperglycemia is typically managed by subcutaneous or intravenous insulin administration. • Blood glucose level less than 180 mg/dL (10.0 mmol/L) is optimal for the ambulatory office setting. • Diabetic patients should be treated as the first patient early in the morning	
Dortch et al. Aesthetic Surgery Journal. 2016 (9) Perioperative Glycemic Control in Plastic Surgery: Review and Discussion of an Institutional Protocol	Practice guideline for care of diabetic patients undergoing plastic surgery with specific procedure examples as well as a generalized protocol from the Mayo Clinic	• Outpatient guidelines: ○ Pre-operative screening to include HbA1c. ○ If HbA1c >8%, refer to primary care physician for optimization. ○ Monitor blood glucose in post-anesthesia unit. ○ Goal of <180 mg/dL following surgery. ○ Patients should be instructed to resume customary monitoring and resume fast acting insulin if discontinued prior to surgery.	• Wound infection • Wound healing • Impaired immunologic defense mechanisms • Increased mortality
Galtier et al. DIAMS study group. J Visc Surg. 2020 (10) Bariatric surgery and the perioperative management of type 2 diabetes: Practical guidelines	Provides results of survey amongst physicians for guidelines of perioperative management for diabetes patients in the specific context of bariatric/metabolic surgery	• Pre-operatively, screening for retinopathy and cardiac ultrasound should be performed. • HbA1c <8% is required in the pre-operative period for most experts screened. • 26.4% and 36.3% of experts determined that metformin should be stopped earlier than other hypoglycemic compounds for 48 and 24 hours before surgery, respectively. • Oral hypoglycemic compounds should be stopped the morning of surgery, and GLP-1 agonists should be stopped 24 hours before the day of surgery (45%) or the day of (25%). • Fast-acting insulin and long-acting insulin are stopped in the morning of the surgery for, respectively, 60% and 45% of the experts. • Post-operatively, insulin pump treatment should not be stopped, basal insulin should be halved, and prandial insulin should be stopped except for severe hyperglycemia patients. • Sulfonylureas should be stopped in immediate post-operative period.	• Microvascular complications
Galway et al. World J Diabetes. 2021 (11)	Provides management guidelines for pre-operative assessment	• In the preoperative phase, target Hba1c should be less than 8%. It is also recommended that the patient's blood glucose	• Postoperative complications: diabetic ketoacidosis, and

Author and Title	Summary	Recommendations	Noted Complications
Perioperative challenges in management of diabetic patients undergoing non-cardiac surgery.	and management for non-cardiac surgery diabetes patients in the pre-operative, intraoperative, and post-operative phases	not exceed 300 mL/dL, that they do not have a hyperosmolar hyperglycemic state, and do not have diabetic ketoacidosis. • Preoperatively, antidiabetic medication should be adjusted or withheld accordingly to prevent accidental hyperglycemic/hypoglycemic episodes (should withhold metformin, glucagon-like peptide-1 agonists, sulfonylureas, and thiazolidinediones on day of surgery, and SGLT2 should be withheld at least 3 days before surgery) • Long-acting insulin should be reduced by 50% on the morning of surgery. Intermediate acting insulin should be maintained the day before surgery, but a 25% or 50% reduction in doses is recommended the night before and the day of surgery. Short acting insulin should generally be avoided on the day of surgery and only be administered according to actual blood glucose levels. • Intraoperatively, insulin should be administered when glucose levels are above 180 mg/dL, and intravenous glucose when the levels are below 70 mg/dL. The general range is from 110 - 180 mg/dL, with an upper limit of 216 mg/dL for patients with poor control.	hyperglycemic hyperosmolar nonketotic state • Acute renal failure, acute myocardial infarction • Longer ICU and hospital stay
Grant et al. Clinical Medicine, Journal of the Royal College of Physicians of London. (12) New guidance on the perioperative management of diabetes.	Practice guideline focusing on the perioperative management of diabetic patients from the UK's Center of Perioperative Care (CPOC)	Referrals for surgery on all patients with diabetes should be evaluated for: • HbA1c within 3 months of referral should be evaluated. • Control of comorbidities and all medications. Before Surgery - Assess and Optimize • Diabetes • Comorbidities - Ensure shared decision making. • Weight Management • Exercise • Smoking Cessation • If HbA1c >69 mmol/mol (8.5%) refer for optimization before undertaking surgery, where clinically safe and possible. Develop individualized plan for: • Pre- and post-surgery medication changes.	• Surgical related infection • Raise plasma glucose levels • Increase insulin resistance • Diabetic ketoacidosis (DKA) • Hyperosmolar hyperglycemic state (HHS) • Hyper- or hypoglycemia

Author and Title	Summary	Recommendations	Noted Complications
		• Day surgery or inpatient surgery. • Timing of surgery - scheduling of surgery should aim to minimize the period of fasting for patients with diabetes. • Communicate plan with patient, primary care, surgical, anesthetic and diabetes teams to ensure pre-operative optimization. On Admission: • Ensure medicines reconciliation maintain capillary blood glucose at 6-12mmol/L document CBG, renal profile, lactate ketones in emergency patients ensure patients with T1D are never denied insulin. Medication Adjustment: • Long-acting or premixed insulin can usually be continued the day before and day of surgery but with a dose reduction (usually between 50%–80% depending on the type of insulin used). A rare but potentially serious and life-threatening association between SGLT-2i and euglycemic DKA has been recognized, the risk of which is increased when there is a restriction to food or fluid intake (such as fasting for surgical procedures). SLGT-2i should, therefore, be withheld in any patient who has been hospitalized for major surgery or acute serious illness. • Ketones levels should be monitored daily, even if asymptomatic with normal blood glucose levels, and the drugs should only be restarted once the clinical condition has stabilized and normal oral intake is established. During Surgery • Glucose should be maintained between 6-12mmol/L. • Capillary blood glucose (CBG) should be checked at induction and at least hourly if on insulin or insulin secretagogues, otherwise a minimum of 2 hourly. • Immediate access to glucose meter, ketone meter and hypoglycemia management.	

Author and Title	Summary	Recommendations	Noted Complications
		Return to Ward • Blood glucose should continue to remain in the target range of 6–12 mmol/L. • Aim for early eating and drinking should enable patients to promptly restore their usual diabetes regimen. • Appropriate use of anti-emetics and analgesia, avoidance of intravenous fluids if able to meet needs orally or enterally, and promotion of mobilization. Discharge • Communicate with patients all medication changes, plan for future diabetes care, importance of self-management.	
Harrop et al. Neurosurgery. 2021 (13) Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines for Perioperative Spine: Preoperative Surgical Risk Assessment	This evidence-based guidelines provides a Grade B recommendation regarding HbA1c levels in diabetic patients undergoing spine surgery.	• Diabetic individuals undergoing spine surgery should have a preoperative hemoglobin A1C (HbA1c) test before surgery and be counseled regarding the increased risk of reoperation or infection if the level is >7.5 mg/dL.	• Infection
Jinjing et al. Diabetes Metab Res Rev. 2021 (14) Chinese clinical practice guidelines for perioperative blood glucose management	Article provides guidelines that are intended to improve perioperative blood glucose management.	• Perform comprehensive assessment of patient's preoperative blood glucose levels and diabetes associated complications that can affect surgical prognosis. • Medical staff should communicate at least once during management of perioperative blood glucose. • Endocrinologist consultation for patients with preoperative acute complications or severe chronic complications of diabetes. • Endocrinologist consultation is recommended for perioperative patients with significant and frequent hypoglycemia, high glucose fluctuations and glucose levels that do not fall within the standard range.	• Surgical site infection • Edema • Prerenal renal insufficiency

Author and Title	Summary	Recommendations	Noted Complications
		• For patients with Fasting plasma glucose (FPG) between 6.1 and 7 mmol/L and high risk of diabetes, oral glucose tolerance test (OGTT) is suggested for measuring the fasting glucose levels and venous blood glucose levels 2 hours after oral administration of glucose. • For patients with high preoperative blood glucose levels but without confirmed diabetes, initial management according to the principles for patients with diabetes is suggested. • Persons with diabetes should have priority for surgery and preferred time for surgery is early in the morning. If surgery cannot be performed in the morning, monitor blood glucose levels continuously in the ward to detect and treat hypoglycemia and metabolic disorders due to fasting. • If random blood glucose is ≥12.0 mmol/L or HbA1c is ≥9%, surgery delay is suggested, for elective surgeries. For patients in emergency surgery showing ketoacidosis or for patients in hyperosmolar coma, recommend that metabolic disorder, pH and osmotic pressure first be corrected. • Anesthesiologist should choose appropriate aesthetic and narcotic drugs according to type of surgery and patients' blood glucose level. During surgery, anesthesiologists should control depth of anesthesia, reduce stress response, rationally use hormones and glucose-containing solutions, actively monitor blood glucose levels and promptly resolve issues that arise. • Target perioperative blood glucose level is 6.0-10.0 mmol/L for longer and medium-length surgeries to prevent hypoglycemia, the target blood glucose level can be increased up to 12.0 mmol/L. Monitor every1-2 hours intraoperatively and every 2-4 hours postoperatively. • For cardiac surgery patients, target is 8.3-11.1 mmol/L and for postoperative blood glucose control is less than 12.0 mmol/L. Monitor every 0.5-1 hours intraoperatively and postoperatively every 2-4 hours. • For neurosurgical patients, target glucose is 5.0-10.0 mmol/L for interoperative control and less than 12.0 mmol/L	

Author and Title	Summary	Recommendations	Noted Complications
		postoperatively. Monitor every 1-2 hours intraoperatively and postoperatively every 2-4 hours. • For patients undergoing "fine surgery" (minimally invasive or microsurgical), the target preoperative blood glucose level is 5.0-7.2 mmol/L. for patients with a long disease course and who have difficulty for glucose control may be increased up to <8.3mmol/L. target for intraoperative blood glucose control is 6.7-11.1 mmol/L and postoperatively <12.0 mmol/L, Monitor intraoperatively every 1-2 hours and postoperatively every 4-6 hours. • For patients in postoperative intensive care or under mechanical ventilation and patients without cardiovascular disease or liver and kidney dysfunction, target glucose level is 7.8–10.0 mmol/L. For patients with cardiovascular and cerebrovascular disease or liver and kidney dysfunction, the target for blood glucose control is 8.0–12.0 mmol/L; however, the upper limit of the target blood glucose level can be extended up to 13.9 mmol/L. The blood glucose levels are monitored every 1–4 hours (2C). • Strengthen staff awareness of the importance of the prevention of hypoglycemia. • Patients should be managed to prevent hypoglycemia and keep blood glucose levels between 5.6 and 10.0 mmol/L. Glucose can be provided intravenously or orally depending on the patient's conditions. • For surgeries less than 1 hour it is not necessary to perform insulin therapy for diabetic patients if blood glucose levels are adequately controlled by previously administered oral antidiabetic agents. During fasting period, sulfonylurea drugs and non-sulfonylurea insulin secretagogues should be stopped. SGLT2 inhibitors should be avoided in case of surgical procedures. • Patients under intraoperative insulin therapy should continue to receive insulin therapy during postoperative fasting period until they start eating, following which oral anti-diabetic agents can be resumed.	

Author and Title	Summary	Recommendations	Noted Complications
		• Diabetic patients with normal renal function do not need to stop taking metformin before surgery. If an intraoperative iodine contrast agent is necessary, metformin should not be taken 24 hours before surgery. For patients with abnormal renal function, metformin should not be taken 48 hours before surgery, and not restarted until renal function is normal. • All staff administering insulin should be properly trained. • Use of insulin perioperatively is allowed and adjusted for the specific patient and level of blood glucose control achieved. • Diabetic patients receiving continuous enteral nutrition or intravenous nutritional support may use variable rate intravenous insulin infusions or continuous subcutaneous insulin infusions for blood glucose management. • Peripheral blood glucose levels should immediately be examined after surgery. • Patients receiving glucocorticoids postoperatively should undergo blood glucose monitoring every hour within 4 hours of administration. For diabetic patients receiving NSAIDs (particularly in combination with biguanides and glitazones), there is a possible risk of oedema and prerenal renal insufficiency caused by insufficient renal perfusion during hypovolemia. In such cases, physicians should closely monitor blood glucose and renal function monitoring. • Establish a team of nurses specializing in diabetes who are fully involved in management of perioperative blood glucose levels. • Hospitals should provide adequate support and education for patients and be integrated into physician training.	
Kheniser et al. J Diabetes Complications. 2018 (15) Diabetes management before, during, and after bariatric and metabolic surgery	Provides guidelines for pharmacological regimens during the preoperative to postoperative period for diabetic patients undergoing metabolic/bariatric surgery.	• A target HbA1c of < 6.5-7.0% is recommended prior to surgery, and 7.0-8.0% for patients with long-term diabetes or are poorly controlled. • Maintaining blood glucose levels between 140-180 mg/dL is recommended. • Adherence to a subcutaneous rapid acting or continuous insulin infusion is recommended when blood glucose levels are <180 mg/dL but > 140 mg/dL (subcutaneous) and above >180 mg/dL (continuous).	• Hypoglycemic and hyperglycemic episodes • Diabetic ketoacidosis (abdominal pain, nausea, vomiting)

Author and Title	Summary	Recommendations	Noted Complications
		• If a patient has been using longer-acting insulins, half of basal dose can be administered in the morning of surgery. • Premixed human insulin is not recommended, and another basal regimen at half the premixed dose during the morning of surgery as a replacement is recommended. • A patient's insulin dosage should be below 0.6 units/kg to reduce risk of hypoglycemic events. • If blood glucose levels on admission are between 140-200 mg/dL, basal bolus regimen at 0.4/kg/day is given (evenly split between basal and bolus). For levels of 201-400 mg/dL, 0.5 units/kg/day are given. If fasting glucose is still >140 mg/dL, basal dose is increased by 20%. Basal insulin is decreased by 20% if hypoglycemic threshold is passed (<70 mg/dL). • Post-operative anti-diabetic regime should be adjusted depending on needs of the patient.	
Kuzulugil et al. Curr Opin Anaesthesiol. 2019 (16) Recent advances in diabetes treatments and their perioperative implications	General perioperative management guideline for diabetes patients with an emphasis on glycemic control measures (avoiding hyperglycemia and hypoglycemia via therapeutic agents). There is also a short section on preoperative glycemic control.	• Optimal blood glucose target for hospitalized patients is approx. 106-180 mg/ml (6-10 mmol/L). • There is significant variability across clinical practices when it comes to anti-hyperglycemic medications. • Metformin can be withheld on the day of surgery. • Sulfonylureas should be ceased before surgery (~24 hour-period). • SGLT2 inhibitors should be ceased before surgery, and administered again postoperatively when patient is feeling well/eating normally. • DPP4 inhibitors, and GLP-1 agonists can be withheld or continued perioperatively without major clinical outcome variance between the approaches. • GLP-1 agonists possibly should be encouraged to be withheld due to some nausea effects. • Improved hospital care delivery standards/clinical processes will help glycemic control.	• Increase in hospital stay • Diabetic ketoacidosis (SGLT2) • Nausea + Vomiting (GLP-1)
Leung et al. Health Serv Insights. 2017 (17)	Perioperative guideline on assessment and management of	• Identification of non-diabetic patients who could possibly develop hyperglycemia due to surgery induced stress. Evaluation of HbA1c should be conducted to distinguish	• Hyperglycemia • Postoperative infection • Poor wound healing • Increased mortality

Author and Title	Summary	Recommendations	Noted Complications
Perioperative Management of Patients with Diabetes	diabetic patients and in regards to surgery, anesthesia, hyperglycemic, medication regiment, transition to ward and discharge.	patients with elevated levels to identify unrecognized diabetes or prediabetes condition from "de novo" stress hyperglycemia. • Perioperative Glycemic Targets - Reference to ADA recommendation of targeting a perioperative glucose target of 80 to 180 mg/dL. • Preoperative Assessment - assessment of glycemic control and any diabetes associated complications. • Comprehensive cardiac evaluation includes resting electrocardiography for intermediate and high-risk surgeries and if cardiac disease is suspected, stress or coronary artery angiography as indicated. • Baseline laboratory date may include measurement of serum creatinine level to assess for chronic kidney disease, HbA1c if not previously available within the past 3 months, and blood glucose level, recommended for patients even without prior history of diabetes to avoid undiagnosed diabetes. • Patients treated with oral medications and/or noninsulin injectable - The morning of surgery, most organizations advise discontinuing oral and noninsulin injectable medications. ○ SGLT-2 inhibitors may increase the risk of volume depletion and DKA and should be withheld the day of surgery. ○ Metformin should be avoided as it may increase the risk of renal insufficiency and lactic acidosis. ○ Thiazolidinediones should be avoided due to potential fluid retention, peripheral edema and congestive heart failure. • Patients treated with insulin - Basal/bolus insulin regimens should be considered to be the most physiologic, as they best mimic normal pancreatic secretory function. • Patients with type 1 diabetes or insulin-treated type 2 diabetes should be instructed to continue their usual meal plan and insulin regimen until the night before surgery. • Perioperative Glucose Monitoring and Insulin Strategies - Blood sugar should be checked before surgery and every 1 to 2 hrs. intraoperatively. Most diabetic patients can be managed with	• Metabolic derangements • Diabetic ketoacidosis (DKA)

Author and Title	Summary	Recommendations	Noted Complications
		subcutaneous insulin perioperatively. Critically ill patients, insulin-treated patients undergoing longer and complicated surgeries or T1D patients should be managed with an intravenous insulin infusion with frequent glucose monitoring (at least hourly) with adjustments to maintain glucose targets. • Transition to Ward and Discharge - Patients should be transitioned to subcutaneous basal/bolus insulin regimen prior to intake of solid food. Insulin Infusion to subcutaneous insulin transitions should overlap at least 1 to 2 hours after first dose of subcutaneous insulin to prevent gap in insulin coverage. For patients previously not treated insulin, a subcutaneous regimen totaling 0.2 to 0.5 units/kg of body weight depending on the patient's insulin sensitivity should be given.	
Livshetz & Nett. Tech. Orthop. 2019 (18) Perioperative Management of Diabetes for Total Joint Arthoplasty: A Consensus Article	Review covering questions of screening, HbA1c level cut-offs, and guidelines for practice in total joint arthroplasty	• Given lack of consensus for HbA1c limits of 7%, <8% seems prudent to mitigate risks. • All patients should be screened for HbA1c levels and orthopedic surgery should be postponed if spot glucose checks result in >200 mg/dL on the day of surgery. • ADA guidelines should be followed for peri-operative glucose control (pre-prandial 80-130 mg/dL and < 180 mg/dL post-prandial).	• Wound complications • Thrombosis • Surgical site infection
Mechanick et al. Endocr Pract. 2019 (19) Clinical Practice Guidelines For The Perioperative Nutrition, Metabolic, And Nonsurgical Support Of Patients Undergoing Bariatric Procedures - 2019 Update: Cosponsored By American Association Of Clinical Endocrinologists/American College Of Endocrinology, The Obesity Society,	Updated clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures.	• Preoperative glycemic control, A1C value of 6.5% to 7.0% or less and peri-procedural blood glucose levels of 80 to 180 mg/dL. • Intra-/perioperative IV insulin is recommended for glycemic control. In type 2 diabetics, postoperatively, the use of all insulin secretagogues (sulfonylureas and meglitinides), sodium-glucose cotransporter-2 inhibitors and thiazolidinediones should be discontinued and insulin doses adjusted to minimize risk of hypoglycemia. Except for metformin and incretin-based therapies, antidiabetic medications should be withheld if there is no evidence of hyperglycemia. Metformin and or incretin-based therapies may be continued postoperatively in patients with type 2 diabetes until prolonged clinical resolution of type 2 diabetes is demonstrated by normalized glycemic targets. Subcutaneous insulin therapy, using a rapid-acting insulin	

Author and Title	Summary	Recommendations	Noted Complications
American Society For Metabolic & Bariatric Surgery, Obesity Medicine Association, And American Society Of Anesthesiologists - Executive Summary		analogue (insulin lispro, aspart, or glulisine) before meals and a basal long-acting insulin analogue (insulin glargine, detemir, or degludec) should be used to achieve glycemic targets (140 to 180 mg/dL) in hospitalized patients not in intensive care (Grade D). In the intensive care unit (ICU), IV regular insulin as part of a standard intensive insulin therapy protocol should be used to control hyperglycemia to a 140 to 180 mg/dL blood glucose target (Grade D). Endocrinology consultation should be considered for patients with type-1 diabetes (T1D), or with T2D and uncontrolled hyperglycemia (Grade D).	
Mumdzic & Munir, Surgery. 2020 (20) Perioperative management of diabetes and corticosteroid supplementation	Peri-operative guidance on peri-operative diabetes management and supplemental corticosteroid treatment	• Pre-operative evaluation should include history, kidney function, blood count and coagulation profile, updated HbA1c. • Refer for expert optimization of glucose control if HbA1c > 8.5% for elective surgeries. • Intra-operative levels of 6-10 mmol/L should be the goal (6- 12 mmol/L is acceptable). • Diet-managed Type 2 diabetics may not require therapy and are not at risk for hypoglycemia, though if they become hyperglycemic they can be managed with fast acting insulin. • Management of glucose should be made with consideration of surgery complexity as to how many missed meals will be experienced.	• Increased postoperative morbidity and mortality
Robinson et al. Anaesth. Intensive Care Med. 2020 (21) Perioperative management of diabetes	Review of perioperative diabetes management with background information, management steps and recommendations on special populations/situations	• Referrals for surgery should include HbA1c in the last 3 months, BMI, eGFR, and accurate medication list. • Thorough pre-operative assessment for cardiovascular disease, diabetic nephropathy, autonomic neuropathy, peripheral neuropathy, diabetic retinopathy, obesity, autoimmune disease, and HIV. • Postpone elective surgery if HbA1c > 69 mmol/mol (8.5%) to confirm optimization and consult with multidisciplinary team to proceed. • Minimize fasting time by early scheduling (first of day or within first 1/3rd of schedule). • Perioperative glucose management plan should be made based on pre-operative levels to adjust medications including insulin.	• Post-operative infection (surgical site or systemic) • Cardiovascular events • Acute kidney injury • Stroke

Author and Title	Summary	Recommendations	Noted Complications
		• Intra-operative levels of 6-10 mmol/L should be the goal (6- 12 mmol/L is acceptable). • Patients should be provided with information on managing their diabetes upon discharge.	
Roth et al. Interdisciplinary Diabetes and Nutrition in Operative Intensive Care Medicine Competence Group. Dtsch Arztebl Int. 2021 (22) Blood Sugar Targets in Surgical Intensive Care—Management and Special Considerations in Patients With Diabetes	Provides blood sugar management guidelines for diabetic patients in intensive care units.	• A target range between 7.8 and 10 mmol/L (140-180 mg/dL) is the goal for diabetic patients in the intensive care unit, as it optimizes clinical outcomes while avoiding hypoglycemia. • Insulin therapy should not be initiated until a level of 10 mmol/L (180 mg/dL). • The range between 4.4 to 6.1 mmol/L (79-110 mg/dL) is not recommended for diabetes patients due to risk of hypoglycemia. • Hyperglycemia and hypoglycemia should be avoided.	• Wound/systemic infections • Immune dysfunction (impaired leukocyte function and phagocytosis) • Oxidative tissue stress, mitochondrial aberration, endothelial dysfunction • Hemodynamic effects (osmotic diuresis/ dehydration, volume depletion, hypoperfusion, electrolyte/acid-base balance disorders
Simha & Shah. JAMA. 2019 (23) Perioperative Glucose Control in Patients With Diabetes Undergoing Elective Surgery.	Description of management of blood glucose in perioperative period with guidance on insulin management	• HbA1c should be checked in all patients. • Postpone elective surgery if HbA1c > 8% and would require intensifying of diabetes management strategies. • Postpone elective surgery in severe hyperglycemia (>250 mg/dL). • Reduce insulin prior to surgery (50-75%), with half- dose on day of surgery if glucose is elevated. • Schedule procedure in the AM to reduce duration of fasting. • Intra-operative management to <180 mg/dL without causing hypoglycemia. • Re-check blood glucose post-operatively, with a goal of pre-prandial 100-140 mg/dL and random 100-180 mg/dL.	• Wound infection • Pneumonia • Sepsis • Cardiovascular events
Song et al. Endocrine. 2019 (24) Critical appraisal and systematic review of	An analysis and comparison of various perioperative management guidelines, an	• Blood glucose level target range is 5-12 mmol/L. • HbA1c, hyperglycemia, and hypoglycemia should be managed. • Blood glucose should be monitored generally once per 1-2 hours for perioperative patients.	

Author and Title	Summary	Recommendations	Noted Complications
guidelines for perioperative diabetes management.	assessment of quality through the AGREE II guideline evaluation tool.	• Oral anti-diabetic drugs (metformin, sulphonylureas, etc.) should be generally discontinued on day of surgery, but strategy and guidelines for this vary significantly. • Insulin therapy should be managed depending on the needs of the patient.	
Stryker. The Journal of Arthroplasty. 2016 (25) Modifying Risk Factors: Strategies that Work Diabetes Mellitus	Peri-operative guidance on checking and managing blood glucose in patients with and without diabetes diagnosis undergoing total joint arthroplasty.	• Peri-operative screening in all patients with >200 mg/dL, further screened for HbA1c. • Goal of <7% HbA1c, though may be higher with individual cases. • Unmanageable levels should be referred to dietician or patient's primary physician. • Short acting insulin or oral regimens withheld on morning of surgery, with long-acting agents or infusion pumps continued. • Post-operative insulin regimens can resume after resumption of regular diet.	• Delayed wound healing • Deep infection • Thrombosis • Mortality
Vervoort et al. J Card Surg. 2022 (26) Sweet victory: Optimizing glycemic control after coronary artery bypass grafting	Presents guidelines on peri and post-operative glycemic control for patients specifically undergoing coronary artery bypass grafting.	• Glycemic control is best achieved with continuous insulin infusions rather than intermittent subcutaneous insulin injections or intermittent intravenous insulin boluses. • Patients with and without diabetes with high serum glucose (>180 mg/dl) should receive intravenous insulin infusions to maintain serum glucose <180 mg/dl for ICU care duration. • Patients with diabetes should receive insulin infusion in OR and for at least 24 hours postoperatively to keep serum levels <180 mg/dl. • Patients who need 3 or more days in ICU due to ventilatory dependency or general heart complications should receive continuous insulin infusion to keep blood glucose <150 mg/dl. • Oral hypoglycemic medications should be restarted in patients who achieved target blood glucose levels if there are not contraindications. • If an intravenous insulin infusion is initiated in the preoperative period, it should be continued throughout the intraoperative and early postoperative period according to institutional protocols to maintain serum glucose ≤180 mg/dl. • A target blood glucose level ≤110 mg/dl should be achieved in the fasting and premeal states after transfer to the floor.	• Sepsis

Author and Title	Summary	Recommendations	Noted Complications
		• Before intravenous insulin infusions are discontinued, patients should be transitioned to a subcutaneous insulin schedule using institutional protocols. • Oral hypoglycemic medications should be restarted in patients who have achieved target blood glucose levels if there are no contraindications. Insulin dosages should be reduced accordingly. • Before discharge, all patients with diabetes and those who have started a new glycemic control regimen should receive inpatient education regarding glucose monitoring, medication administration (including subcutaneous insulin injection if necessary), nutrition, and lifestyle modification.	
Vongsumran et al. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 13 (pp 2593-2601), 2020 (27) Standardized glycemic management versus conventional glycemic management and postoperative outcomes in type 2 diabetes patients undergoing elective surgery.	A review of the efficacy of Conventional perioperative glycemic control protocol (CG) versus Standardized glycemic control protocol (SG). There was no significant difference in the percentage of hypoglycemic events between the CG and SG protocols	• Keeping blood glucose at less than 180 mg/dL but above 108 mg/dL can reduce mortality rates in critically ill surgical patients. Patients with blood glucose levels above 200 mg/dL perioperatively have an increased rate of infection. • Per FDA - SGLT-2i should be discontinued at least 3 days prior to scheduled surgery to reduce the risk of ketoacidosis.	• Mortality • Infection
Wang et al. Clinical Neurology and Neurosurgery, 2021 (28) Perioperative optimization for patients undergoing elective spine surgery.	General perioperative guideline on management of patients in regard to medications, diabetes, hypertension, smoking, renal function, BMI, psychosocial aspects, and frailty.	• HbA1c goal of < 7% • Pre-prandial glucose 90-130 mg/dL • Post-prandial glucose < 180 mg/dL • First-start surgical case (early in the surgery day). • Insulin Glucose Tolerance Test (GTT), IV management perioperative) for >200 mg/dL. • Continue home insulin, discontinue atypical hyperglycemic agents. • Cancellation of procedure if in diabetic ketoacidosis or >400 mg/dL.	• Delayed wound healing • Infection • Thrombosis • Mortality

Author and Title	Summary	Recommendations	Noted Complications
Seisa et al. Journal of Clinical Endocrinology and Metabolism, 2022 (29) A Systematic Review Supporting the Endocrine Society Clinical Practice Guideline for the Management of Hyperglycemia in Adults Hospitalized for Noncritical Illness or Undergoing Elective Surgical Procedures.	This article supports the development of clinical practice guidelines for management of hyperglycemia in adults hospitalized for noncritical illness undergoing elective surgical procedures.	• Continuous glucose monitoring. • Combine neutral protamine hagedorn (NPH) and basal-bolus insulin. • Emphasize inpatient diabetes education. • Achieve preoperative HbA1c level < 7% when possible. • Hospitalized patients with type 2 diabetes and mild hyperglycemia can be treated with glucagon-like peptide-1 agonists or dipeptidyl peptidase-4 inhibitors if indicated. • All findings were associated with a low or very low level of certainty. Additionally, several factors supported opposite recommendations depending on the outcome measured. This emphasizes the need for shared decision making and consideration of all available factors.	• Length of hospital stay • Hypoglycemia and hyperglycemia events • Hospital readmissions
Williams et al. Journal of Patient Centered Research Reviews, 2023 (30) Impact of Perioperative Dexamethasone on Hospital Length of Stay and Glycemic Control in Patients With Type 2 Diabetes Undergoing Total Hip Arthroplasty.	Evaluation of length of hospital stay in patients with type II diabetes when prescribed dexamethasone perioperatively.	• Dexamethasone can be safely administered to patients with type II diabetes during surgical procedures to relieve subsequent pain and nausea. • Those taking insulin may benefit from having their postoperative care managed by diabetes specialists due to increased insulin resistance in the first 24 hours following surgery.	• Elevated blood glucose levels

(2) Safety and Effectiveness Literature Search

Initial screening was performed on 690 titles and abstracts resulting in the selection of 133 publications for full-text review. After full text review, articles were selected for inclusion based on safety, effectiveness, or as meta-analyses. The following number of publications were selected for each category:

- Safety: 26 publications. Several studies resulted in multiple publications. Safety information was extracted from the publication with the longest follow-up from each study that included comprehensive adverse event information and is included in Table III.2.
- Effectiveness: 15 publications. Several studies resulted in multiple publications. Effectiveness data was extracted from all publications and included in total for each cohort. This information is reported in Table III.3.
- Meta-analyses: 8 publications reported meta-analyses of studies of SCS to treat DPN. The reports are summarized in Table III.4.

Table III.2. Summary of Safety Results in Selected Studies

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
Tesfaye et al. 1996 (31), Daousi et al. 2005	Prospective observational study for SCS use for the treatment of DPN. Included a double-blind test stimulation period.	10 patients, 8 received permanent implants	3.3-year mean, up to 7 years	3 patients died from myocardial infarction at 2 months, 2 years and 4 years post-implant. Lead migration requiring revision occurred in 2 patients, 2 patients required antibiotics for superficial wound infection, 1 system removed after 4 months for system failure, 1 hematoma at implant site without clinical impact, 1 lead failure due to trauma required replacement.	Relevance: First study evaluating SCS for DPN specifically. Long term follow-up of safety/complications. Limitations: Small, single arm open label study. No comparator.
TenVaarwerk et al. 1999 (32)	A retrospective, multicenter study of patients treated with spinal cord stimulation between 1987 and 1997	517 patients with angina pectoris and a permanent SCS implant, 14% identified as having Insulin Dependent Diabetes Mellitus	Median follow-up was 23 months (range of 0 to 128 months)	Insulin dependent diabetes was the only important risk factor between the groups (survivors vs non-survivors, p = 0.05). Diabetes (p = 0.01) was significantly correlated with mortality.	Relevance: Review of diabetes as a co-factor associated with mortality. Determination that there was a significant difference in mortality in the diabetic population. Limitations: Retrospective, follow-up times variable, no separate DPN population. No analysis of diabetes related to SCS complications.
Petrakis et al. 1999 (33)	Retrospective study of diabetic patients with peripheral arterial occlusive disease (PAOD) to evaluate pain relief and reduction of amputation rate with SCS	64 diabetic PAOD patients	58 months mean follow-up (20-128 months)	Of 14 patients with rest pain and no lesions (most similar to the DPN population being evaluated in this study), 1 patient required limb amputation, and one had a generator infection leading to removal of the device. Overall diabetic cohort had 8 battery replacement procedures following normal end of device life, 2 lead migrations requiring lead revision, 2 Infections requiring explant.	Relevance: Early study describing SCS in a diabetic population. PAOD is common in diabetic patients and frequently overlaps with DPN. Limitations: Open label, no comparator.
de Vos et al. 2009 (34)	Prospective, open label, observational trial for diabetic patients with chronic pain	11 patients enrolled, 9 received permanent implant	30 months	Surgical revision due to inadequate connection between the lead and the extension cable in 2 patients. After revision the pain relief reappeared in both patients. One patient had a mild infection that was	Relevance: Few safety events which were resolvable.

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
				treated easily with antibiotics, without any influence on the SCS treatment. One death which was reported as unrelated to SCS.	Limitations: Open label design. Single center, small trial without comparator.
Mekhail et al. 2011 (35)	Retrospective review of case series in patients with SCS for intractable pain (Failed Back Surgery Syndrome, Complex Regional Pain Syndrome (CRPS), Peripheral Vascular Disease (PVD), visceral pain, neuropathy over a 5-year period	707 patients, 56 patients were diabetic	Variable, from 3 months to 7 years	Pain at the generator site (86), seroma without infection (1), lead migration (119), lead connection failure (50), and lead break (33). There were 32 (4.5%) patients that had infections. Of those with diabetes (56 patients total), 5 (9%) developed infections.	Relevance: Large evaluation of SCS experience over a 5-year period with a range of pain etiologies. This article reports safety issues primarily related to infection and device failures. Diabetic patients were noted to have a higher, though non-significant, rate of infection. Long-term follow-up included. Limitations: No specific effectiveness data provided. Retrospective nature of study can lead to bias. Small diabetic population.
Pluijms et al. 2012 (36), Pluijms et al. 2015 (37), Slangen et al. 2013 (38), Slangen et al. 2014 (39), van Beek et al. 2015 (40), van Beek et al. 2018 (41) Zuidema et al 2022 (42)	Prospective, randomized, open-label multicenter RCT to assess the effectiveness of SCS in combination with best medical treatment (BMT) compared with BMT only in patients with PDPN in the lower limbs. Patients were pooled from all subjects reported in Pluijms 2012 and Slangen 2014	49 patients enrolled 40 patients had a successful trial and received a permanent implant 19 continued use of the device at 8 or more years and consented to participate in the study	Up to 10 years	• 13 battery replacements due to depletion (5 had 2 replacements) • 10 pain in the battery pocket (1 revision without complete resolution) • 9 reported uncomfortable stimulation • 6 device removals due to loss of efficacy • 5 lead migrations with revisions • 4 lead failures which were replaced • 2 infections leading to explant • 1 participant had a dural puncture during attempted trial lead implantation. 3 days later the patient had a subdural hematoma causing midline shift and eventual death • During the 8-10 year follow-up, many patients needed either one (53%) or two (24%) replacements the original non-rechargeable IPG	Relevance: Patients from a randomized, multi-center, 2 arm trial of SCS in patients with DPN compared to best medical treatment were combined with a cohort of patients in a single arm, open label study. Long term follow-up to 10 years. Many device explants happened in the first two to three years; however, after this period, device explants were less frequently observed. The ten-year survival probability was equal to 0.66 (95% CI: 0.53–0.83). Limitations: Open label. No control group for the 5- or 10-year follow-up period. Study enrollment over 4 years, potential for increased expertise in surgeons or

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
				• There were no new AEs reported in the 8-10 year follow-up	nurses who implant or change SCS settings.
de Vos et al. Feb 2014 (43)	Open label study in patients with 6 months experience SCS tonic stimulation to determine efficacy of switching to burst.	48 patients total, 12 with DPN	2 weeks	1 patient had worsening pain; side effects mentioned by patients were headaches (3), dizziness, and the sensation of “heavy legs" (2).	Relevance: First study assessing a switch to burst after having tonic stimulation. This is very different from patients who started with burst. Many missed the paresthesia as a feedback signal that the SCS system is functioning. Limitations: Only 2-week evaluation. No opportunity to change stimulation. Single center study with small number of DPN patients. Potential selection bias by reviewing patients with implants. Safety data not specific to DPN population.
de Vos et al. Nov 2014 (44)	Open label, randomized trial with conventional medical practice (control) compared to SCS	60 patients with DPN were enrolled and randomized to SCS (n = 40) or control (n = 20) treatment. 3 SCS patients did not have successful trial stimulation, and 1 additional patient was withdrawn after deciding to enter into another study. 36 completed 6-m f/u.	6 months	AEs related to the implantation included: pain due to the IPG (2), lead migration (1), perceived incomplete overlap of the paresthesia with the painful area during trial stimulation leading to a second electrode lead placed (1); infection during trial stimulation (1); coagulopathy in 1 patient complicated the implantation procedure and prolonged hospitalization. Potentially unrelated complications included 2 infections resulting in unstable blood glucose levels, 1 femur fracture, and 1 cardiac arrest. In the control group, there were 2 infections, 1 carotid artery stenosis, 1 myocardial infarction, 1 atrial fibrillation episode, and 1 coronary bypass surgery.	Relevance: Randomized trial compared to BMT. Detailed adverse events information including relatedness. The authors indicate the need to carefully monitor blood glucose levels in the presence of infection. Limitations: Open label design with limited follow-up (6 months). Patients were aware that they would be offered trial SCS after 6 months. It cannot be ruled out that some of the data collected in this group was biased by this prospect.

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
Bir et al. 2016 (45)	Retrospective study, not specific to DPN. However, there is an analysis of the effect of diabetes on revision free survival.	141 cases where participants had an SCS system implanted	Mean follow-up was 31.49 months	Revision free survival (RFS) in non-diabetics was 43 months, in diabetics was 35 months. The effect of diabetes on RFS was not statistically significant.	Relevance: Comparison of revision free survival curves with diabetes as a co-factor. Diabetes was not associated with a significant difference. Limitations: Retrospective (limitations on data collection, follow-up times are variable), not specific to DPN.
Denisova et al. 2016 (46)	Prospective, open label trial for patients with chronic spinal cord pain	Total of 136 patients with neuropathic pain syndrome underwent test stimulation, 75 received the permanent implant SCS.	6-18 months	2 SCS removals due to pain at generator implant site, 4 lead migrations required surgical revision/repositioning	Relevance: General SCS safety rates. Limitations: No data specific to the DPN population except for the statement that significant regression of pain was achieved in patients with diabetic neuropathy.
Hoelzer et al. 2017 (47)	Multi-center, retrospective review in patients treated for FBSS, CRPS, Post-Herpetic Neuralgia, and other chronic pain conditions	2737 patients who had SCS implantation between Jan 2007 and June 2014 16.5% had diabetes	1 year	Primary placement infection rate: 2.19% Revision infection rate: 3.09% Total infection rate: 2.45% Rate of infection when no occlusive dressing was applied was 3.86% vs. 1.69% when an occlusive dressing was used. Rate of infection was 1.78% for patients who received post-operative antibiotics (78.3%). No post-operative antibiotics rate of infection was 4.09%. Analysis of surgical site infection association with diabetes. Infection rate for patients with diabetes: 1.99% without diabetes: 2.54% (p = 0.49)	Relevance: Large review that analyzed diabetes as a co-factor for prediction of surgical site infection. Diabetes did not demonstrate a statistically significant influence on the rate of infection. Applying a sterile occlusive dressing while in the operating room significantly decreased the rate of infection generally. Limitations: Retrospective design, reporting bias, and the inherent restraint to identify causation. Authors found lack of continuity for some of the categorical variable data related to inconsistent reporting.
Falowski et al. 2019 (48)	Retrospective analysis of patients with SCS implant from 2009-2014	26,854 patients had a record of SCS generator implant or replacement during	12 months	3.11% of all SCS patients (206/6615) experienced an infection event within 12 months after their initial implantation date. The difference of infection rates between the	Relevance: A large retrospective study based on real-world data which provides valuable information on infection rates associated with SCS implants. There was

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
	included in a payer database to estimate rates of infection and other safety risk factors.	the study period. The final study population was 6615 patients after applying eligibility criteria. 5563 (84.1%) patients were identified as the initial group (patients with no evidence of prior SCS implant), and 1052 (15.9%) patients were identified as the replacement group (patients with evidence of prior SCS implant).		initial group (3.09%; 172/5563) and the replacement group (3.23%, 34/1052) was not statistically significant (p = 0.8104). Of those that reported an infection in the initial group, 4.44% of them had type 1 diabetes while 3.41% of those without infection also had type 1 diabetes. Of those that reported an infection in the initial group, 25.60% of them had type 2 diabetes while 22.95% of those without infection also had type 2 diabetes. There was no difference in the rate of diabetes between those that had infections and those that did not.	no difference in the rate of diabetes between those that had infections and those that did not. Limitations: Uncertainty in the results stems from whether accurate occurrence of infection as well as the presence of comorbidities was adequately documented and coded. Also, there is a lack of detailed information about the infection including exact cause of the infection other than it being device related, and severity of infection.
Galan et al. 2020 (49)	Patients with DPN were reported separately from a larger prospective, single arm, multicenter, early feasibility study that evaluated SCS in patients with peripheral polyneuropathy.	9 patients with DPN of the lower limbs underwent a SCS trial stimulation, with 8 undergoing permanent implantation. 7 attended the 12 month follow-up visit	12 months	Events considered procedure related: • 1 implant site dehiscence • 1 leg pain • 1 implant site seroma Events considered non-procedure related: • 1 hematuria • 1 erectile dysfunction • 1 hepatic failure • 1 clostridium difficile infection • 1 abdominal pain • 1 intra-abdominal hemorrhage	Relevance: DPN patients reported independently with detailed AE information. Limitations: Post-hoc analysis, limited samples size, therefore no statistical analyses performed. Adverse event rates are difficult to assess due to the small sample size.
Antonovich et al. 2021 (50)	Single center, retrospective analysis of SCS reoperation rates for leads (paddle vs percutaneous).	291 patients 67% had a history of back surgery, 22.34% had diabetes	Up to 10 years	89 patients required 1 revision (31.58%), 20 required 2 or more revisions (1.72%) 35.59% of participants with paddles needed revision, 47.17% of participants with cutaneous leads needed revision	Relevance: Large data set that analyzed diabetes as a co-factor. No association between diabetes and lead/paddle type in time to re-operation. Use of leads associated with lower infection rates in the general SCS population. Limitations: Single center, retrospective

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
				Overall infection rate of 1.95%. Paddles were associated with 3x higher rates of infection. A diagnosis of diabetes was not associated with reoperation (univariate Hazard Ratio = 0.70; p = 0.197).	study. No detailed AE data for diabetic population. Study reported a potential for charting errors, misinterpretation of charts, errors gathering data.
Petersen et al. 2021 (51), Petersen et al. 2022 (52) Peterson et al 2022 (53)	Prospective, multi-center, open label, randomized trial 10kHz stimulation was compared with conventional medical management 12 month follow-up data included in two secondary publications (Petersen et al., 2022 and Petersen et al., 2022)	216 patients were randomized at 1:1 ratio (103 control group and 113 in the treatment group) 104 patients had a trial stimulation, 90 subjects received a permanent implant 187 patients completed 6-month follow-up visits	6 - 12 months	18 study-related AEs in 14 subjects (12.4% of total study subjects in the treatment group): • 8 procedure-related infections (5.2%): three resolved with conservative treatments and patients continued in the study, five (3.2%) required device explant with 1 receiving a new implant after the infection resolved • 3 revisions; 2 for IPG site revision (1.3%), 1 for lead migration (0.6%); all three continued in the study • 2 wound dehiscence • 1 each of impaired healing, device extrusion, incision site pain, IPG site discomfort, lead migration, contact dermatitis, urticaria, radiculopathy, uncomfortable stimulation, gastroesophageal reflux, myalgia, arthralgia, and hyporeflexia and 2 SAE (i.e., explant)	Relevance: Multi-site study, large RCT which includes a comprehensive list of all study related AEs. Detailed AE information was provided including determination of relation to device or not. Limitations: It is unclear if multiple adverse events occurred in the same patient and limited information is provided on the reasons for explant. Long-term follow-up was open label.
Goel et al 2022 (54)	Retrospective analysis of reasons for SCS related hospital readmission	3,668 patients from the National Readmissions Database (NRD) were included	30 days	• The 30-day readmission rate following the SCS implantation procedure was 7.7%. • Readmissions for uncontrolled diabetes accounted for 2.38% of all admissions • A univariate analysis determined that diabetes was a significant predictor for readmission generally (OR - 1.484, p=0.020).	Relevance: Evaluates reasons for readmission within 30 days of SCS implantation in 3,668 patients in a database that pulls from 28 states. Uncontrolled diabetes was recognized as a factor that contributed toward readmission rates generally but was not a predictor of readmission following SCS surgery.

Publication	Study Design	N	Follow-up period	Safety data	Relevance and Limitations
					Limitations: Focus on all SCS implantation, no data reported for a DPN population alone. Limited follow-up. Many revision surgeries happen in the first two years, so this evaluates a percentage of the population that has revision surgeries.
Provenzano et al 2022 (55)	Retrospective study at a single center to determine the prevalence of *S. aureus* colonization for SCS surgical patients and to identify specific at-risk patient populations.	232 patients underwent 396 unique neuromodulation procedures	Minimum 6 months	• Patients were screened for *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) prior to surgery. • 23.3% of patients were colonized with *S. aureus* (4.3% with MRSA and 20.2% for MSSA) • No postprocedural SSIs were identified. • The only co-morbidity that was significantly associated with MRSA colonization was anxiety, and hypothyroidism was the only co-morbidity associated with MSSA MRSA: methicillin-resistant *S. aureus* MSSA: methicillin-sensitive *S. aureus*	Relevance: Large data set that analyzed diabetes as a co-factor. No association between diabetes and *S. aureus* colonization. Many of the previously associated risk factors/co-morbidities did not show an association with MRSA or MSSA colonization. Limitations: Single center, retrospective study. No patients in this study had surgical site infections, so no conclusions can be made for the diabetic patient population.

Table III.3. Summary of Effectiveness Results in Selected Studies

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
Tesfaye et al 1996 (31); Daousi et al 2005 (56)	Prospective observational study for SCS use for the treatment of DPN. Included a double-blind test stimulation period.	10 patients received trial stimulation, 8 received permanent implant	14 months to 7.5 years	Trial success: 80% Statistically significant pain relief of both background and peak neuropathic pain (VAS Pain scores, McGill Pain Questionnaire) was achieved at 3 and 6 months and at the end of the initial study (6-20 months). Average 'peak' pain reductions: • 3 months: 40.8% • 6 months: 47.0% • End of initial study: 56.2% • 3.3 years: 57.5%% • 7.5 years: 36.2% Percent of patients able to achieve ≥50% reduction in 'peak' pain: • 3 months: 42.9% (3 of 7) • 6 months: 57.1% (4 of 7) • End of initial study: 71.4% (5 of 7) • 3.3 years: 66.7% (4 of 6 remaining) • 7.5 years: none (all patients were experiencing pain relief, with a range of 30-45% reduction in pain).	Relevance: First study evaluating SCS for DPN specifically. Long term follow-up. Limitations: Small sample size with only 4 patients completing 7.5 year follow-up, single arm open label study. No comparator.
de Vos et al. Feb 2014 (43)	Open label study in patients with 6 months experience SCS tonic stimulation to determine efficacy of switching to burst.	48 patients total, 12 with DPN.	2 weeks	Tonic stimulation caused 37% mean pain reduction. Burst stimulation caused an additional 25% reduction in pain (52% total). Pain reduction was best in patients with DPN (77%). 8 of 12 experienced additional pain reduction. Several patients indicated that they actually liked the paresthesia. The loss or change of the paresthesia and the inability to increase the stimulation amplitude and thereby the	Relevance: First assessment of switching to burst after having tonic stimulation. This is very different from patients who started with burst. Many missed the paresthesia as a feedback signal that the SCS system is functioning despite meaningful additional pain relief. Limitations: Only 2-week evaluation. No

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
				paresthesia intensity led some patients to prefer tonic stimulation over burst stimulation, in certain cases even despite of the larger pain reduction. In addition, some patients did not perceive the paresthesia as particularly comfortable but were able to shift their attention from the pain to the paresthesia and therefore appreciated it as a distraction from the pain. Success criteria were not established.	opportunity to change stimulation. Single center study with small number of DPN patients. Potential selection bias by reviewing patients with implants.
de Vos et al. Nov 2014 (44), Duarte et al. 2016 (57)	Open label, randomized trial comparing conventional medical practice to SCS	60 patients with DPN were enrolled and randomized to SCS (n = 40) or control (n = 20) treatment. 3 SCS patients did not have successful trial stimulation, and 1 additional patient was withdrawn after deciding to enter into another study. 36 completed 6-month follow-up.	6 months	Trial stimulation success: 93% At 6 months 25 (63%) had 50% or greater reduction in pain (VAS) compared to control (5%); $p<0.001$. Moderate reductions (30–50%) were reported by three patients (8%), minimum reductions in pain intensity (10–30 %) were reported by four patients (10%). 16 had more than 75% reduction (40%). There was also a significant reduction in analgesic intake in the SCS group. Average pain relief at 6 months: SCS 57.5%; control: 0% Patients also experienced significant improvements in Quality of Life as measured by the EQ-5D utility scores including mobility, usual activities, pain/discomfort and anxiety/depression (SCS: 0.39 improvement, control: 0.00 improvement).	Relevance: Randomized controlled trial. Data shows meaningful improvements in pain reduction, mobility, and anxiety/ depression. Randomized trial comparing to conventional medical practice. Limitations: Open label design. Patients were aware that they would be offered trial SCS after 6 months. It cannot be ruled out that some of the data collected in this group were biased by this prospect. Follow-up limited to 6 months. Lack of individual patient data.
Slangen et al. 2014 (39), van Beek et al. 2015 (40)	Prospective, randomized, open-label, multicenter RCT to assess the effectiveness of SCS	36 randomized patients (22 for SCS and 14 for BMT) 17 of 22 had a positive	2 years	Trial success rate: 77% Success defined as ≥50% relief of pain intensity on an NRS for 4 days or a score of ≥6 on a 7-point Likert scale (1 = very much worse, 6 = much	Relevance: RCT to compare SCS against BMT. Includes BMT patients who were able to crossover to the SCS arm. Multicenter. Data shows meaningful

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
	in combination with best medical treatment (BMT) compared with BMT alone in patients with DPN in the lower limbs.	trial period and went on to permanent SCS implantation. 1 withdrew after infection and removal of the SCS implant.		improved and 7 = very much improved) of the PGIC scale for pain and sleep. At 6 months: • 13 of 22 (59%) SCS patients achieved success, 1 out of 14 (7%) BMT patients achieved success • 9 (41%) SCS patients and 0 in the control group had ≥50% reduction in pain on NRS • 12 (55%) SCS patients scored ≥6 (much improved) on the PGIC for pain and 8 (36%) scored ≥6 on the PGIC scale for sleep. No patients in the control group showed any difference in the PGIC scores. Mean pain score reduction on the NRS at 6 months was 3.1 for the SCS group (no change for BMT). Van Beek et al 2015 reported long term efficacy data out of the 17 successful trial stimulation patients. At 2 years, 8 (47%) and 6 (35%) patients reported a 50% pain reduction during day and night, respectively. Clinically significant improvements on the PGIC for pain and sleep were reported by nine (53%). Treatment success of SCS was observed in 11 out of 17 patients (64.7%). Average pain reduction at 12 months: 43.8% (day), 46.2% (night).	effects in pain reduction over a 2 year follow-up. Limitations: Open label. No control group for the 2-year follow-up period.
de Vos et al. 2009 (34)	Prospective, open label, observational trial for diabetic patients with chronic pain.	11 patients enrolled, 9 received permanent implant	30 months	Trial stimulation success: 82% At 3 and 6 months: • 50% or greater pain relief was achieved in six patients (55%)	Relevance: Good long-term effectiveness seen in patients. Limitations: Open label design. Single center, small trial without comparator.

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
				• 30–50% pain relief was seen in two patients (18%) • Average pain score was 77 at baseline and 34 at 6 months after implantation to yield an average pain reduction of 55.8%. After 12 months: • 50% or greater pain relief was achieved in seven patients (64%) • 30–50% pain relief was seen in one patient (9%) • Average pain score was 23 at 12 months to yield an average pain reduction of 70.1%. After 30 months: • 50% or greater pain relief was achieved in six patients (55%) • 30–50% pain relief was seen in one patient (9%) • Average pain score was still 23 at 30 months to yield an average pain reduction of 70.1%.	
Pluijms et al. 2012 (36), Pluijms et al. 2015 (37), Slangen et al. 2013 (38)	Prospective, open-label, single center cohort study on the use of SCS in patients with DPN.	15 patients enrolled (ITT population), 11 patients received permanent implants after trial stimulation.	36 months	Trial success: 73% Clinically relevant pain reduction was defined as ≥50% decrease of pain intensity. Success of SCS treatment was defined as clinically relevant pain relief on 1 or more of: pain daytime, pain night, peak pain, or PGIC. Overall success rates were 67% of patients (10 of 15) after 1 year of SCS treatment, 40% (6 of 15) at 24 months and 47% (7 of 15) at 36 months*. SCS treatment was also associated with improvement of sleep in 47% of patients (7 of 15) at 12 months.	Relevance: Long term follow-up of DPN cohort that received SCS. Data shows meaningful effects in pain reduction over a long period of time. Limitations: Open label, single arm, single center study with a small number of patients.

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
				After 12 months of SCS treatment, daytime pain intensity was reduced by ≥50% in 7 patients (47%), nocturnal pain intensity was reduced by ≥50% in 3 patients (20%), and peak pain intensity was reduced by ≥50% in 3 patients (20%). Eight patients (53%) reported painful symptoms to be "much improved" or "completely resolved." Treatment success was seen in 10 patients (67%) at 12 months. Improvement in QoL was seen in 47% of patients at 12 months, 40% at 24 months and 47% at 36 months. *Long term efficacy results reported by Slangen et al 2013 changed success calculations to compare against only those with a successful trial stimulation. For clarity, these numbers have been recalculated to match the 12-month values reported in the original publication.	
Petrakis et al. 1999 (33)	Retrospective study of diabetic patients with peripheral-arterial occlusive disease (PAOD) to evaluate pain relief and reduction of amputation rate.	64 diabetic PAOD patients	20–128-month range: (58 months on average)	Of 14 patients with pain at rest, >75% pain relief or more was seen in 11 patients (79%). 1 additional patient had >50% pain relief.	Relevance: Early study describing SCS in a diabetic population. PAOD is common in diabetic patients and frequently overlaps with DPN. Shows meaningful improvement for pain relief. Limitations: Limited to patients with pharmacological failure and high pain levels. Open label, no comparator.
van Beek et al. 2018 (41)	Multi-center cohort study of SCS to treat DPN with analyses of predictors of success.	49 enrolled patients, 40 patients received a permanent implant.	5 years	Adjusted NRS pain score reductions of 50% or greater during the day or night was observed in: • 1 year: 42% (15 of 36) day, 36% (13 of 36) night • 2 years: 43% (15 of 35) day, 40% (14 of 35) night	Relevance: 5-year follow-up of two studies including one multi-center RCT. Also includes cross-over patients. High levels of treatment success in many patients out to 5 years. Limitations: No control groups for long-term data. Loss to follow-up for some

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
	Combined cohorts from Puijms 2012[7] and Slangen 2014[10]			• 3 years: 47% (16 of 34) day, 35% (12 of 34) night • 4 years: 37% (11 of 30) day, 33% (10 of 30) night • 5 years: 36% (8 of 22) day, 32% (7 of 22) night The percentage of patients reporting (very) much improvement on the PGIC scale for pain and sleep were: • 1 year: 72% and 53% (26 and 19 of 36) • 2 years: 54% and 37% (19 and 13 of 35) • 3 years: 53% and 29% (18 and 10 of 34) • 4 years: 53% and 47% (16 and 14 of 30) • 5 years: 50% and 32% (11 and 7 of 22) Treatment success (SCS treatment success was defined as ≥50% pain relief on the basis of day and night NRS pain score for 4 days or a PGIC score for pain and sleep of ≥6 on a 7-point Likert scale (1 = very much worse, 7 = very much improved) was observed in: • 1 year: 86% (31 of 36) • 2 years: 71% (25 of 35) • 3 years: 77% (26 of 34) • 4 years: 67% (20 of 30) • 5 years: 55% (12 of 22) Average pain reduction at 12 months is 43.3% (day), 41.8% (night).	long-term time points may bias conclusions.
Kumar et al. 1996 (58)	Case series of patients with pain neuropathies.	30 patients presenting with various peripheral neuropathies (4 upper-limb, 17 thoracic, 9 lower-limb) treated with SCS. 4 patients had diabetic	Average 87 month follow-up (range of 36 – 149 months)	Of all 4 patients with DPN reported ≥50% pain relief at one year. After one year, one patient developed upper-limb pain that was not targeted with the SCS which may have led to a decrease in the perception of pain	Relevance: Very long-term follow-up showing long term efficacy. Early study that reported on DPN patients specifically. Limitations: Small case series in a range

Publication	Study Design	N	Follow-up period	Effectiveness data	Relevance and Limitations.
		peripheral neuropathy. 19 patients underwent permanent implantation after responding positively to trial stimulation.		relief resulting in 1 failed treatment (≤50% pain relief) after one year.	of peripheral neuropathies. Not randomized or blinded.
Zuidema et al 2022 (42)	Prospective, randomized, open-label multicenter RCT to assess the effectiveness of SCS in combination with best medical treatment (BMT) compared with BMT only in patients with PDPN in the lower limbs. Long term follow-up of Pluijms 2012 and Slangen 2014	40 patients received a permanent implant, and 19 continued to use the device at 8 or more years and consented to participate in the study	8 – 10 years	Mean NRS scores for pain intensity during the day and night significantly decreased by 2.3 ± 2.5 and 2.2 ± 2.4 points, respectively, compared to baseline. 57.9% (day) and 53.3% (night) of patients had ≥ 30% reduction in pain intensity. 26.3% (day) and 33.3% (night) of patients had ≥ 50% reduction in pain intensity. Stimulation pulse width widely ranged from 150 to 450 µm. For stimulation frequency, most patients (65%) were stimulated at the default frequency of 30 Hz, but higher frequencies up to 60 Hz were also used. Most patients (82%) needed a maximum of eight adaptations (maximum one per year) during the follow-up time. No differences were observed regarding the secondary outcomes (i.e., QoL, depression, sleep quality).	Relevance: This is the first study with follow-up out to 10 years in more than a few patients. Long term efficacy is preserved in patients that do not fail in the earlier stages (first 1-2 years). Limitations: The only available data at this late time point was from a subset of patients that still have their SCS implanted at this stage. Open-label follow-up.

Table III.4. Summary of Safety and Effectiveness Conclusions in Selected Meta-Analyses

Publication	Study Design	N	Safety Conclusions	Efficacy Conclusions
Hou et al. 2016 (59)	Evaluation of literature to support the use of burst stimulation in the treatment of chronic pain	5 Manuscripts reviewed, 1 discussed DPN	No severe complications described. Only dizziness, headache or a sensation of heaviness or warmth in the legs.	Not enough evidence to recommend for or against use of burst to treat chronic pain or DPN. More high-quality evidence is needed.
Raghu et al. 2021 (60)	Meta Analysis of neuromodulation for DPN. MEDLINE and Embase were searched for appropriate articles. Results were screened by 2 independent reviewers. RCT data was pooled and compared statistically using the inverse variance method and expressed as mean differences. The Cochrane risk of bias tool was used to assess bias.	32 publications including 21 tonic SCS, 2 high frequency SCS, 2 burst SCS, 7 other stimulation modes	Risk of failing therapeutic trial was 16%, and risk of infection was 4%. Risk of lead problems requiring surgery to resolve was 13%: 4% per year of follow-up. IPG replacement was 0% at six months, 12% at two years, 17% at three years, and 45% at five years. Following "permanent" implantation, likelihood of explant was 20% by five years. One patient died from subdural hematoma.	In the two RCTs (n=59) SCS was shown to be superior to BMT at six months. Significant improvement in pain from baseline at 6-and 12-month post-operative follow-up in SCS case series by mITT and PPA, respectively. Long-term case follow-up demonstrates that clinical benefit appears to continue for many years. Mean difference in pain score reduction (0-100 scale) of 37.84 (95% CI 28.83 to 46.85; I2 = 0%). Pooled mean difference for EQ5D = 0.16 (CI 0.02 to 0.30; I2=0%) and EQ-VAS = 11.21 (CI 2.26 to 20.16)
Duarte et al. 2021 (61)	Systematic Review to identify RCTs that studied SCS in DPN. Search was carried out on Embase, MEDLINE and CENTRAL.	2 RCTs with 93 total patients and additional 2 long term follow-up articles	Treatment-related adverse events were reported narratively, but no safety related calculations or conclusions were made.	The authors found a statistically significant reduction in pain intensity: pooled mean difference -3.13, 95% CI -4.19 to -2.08, I^2 = 0% on SCS treatment compared with BMT. There was also a significant increase in patients that achieved at least a 50% reduction in pain intensity with SCS: pooled risk ratio 0.08, 95% CI 0.02-0.38, I^2 = 0%. Risk of Bias assessment using the revised Cochrane risk of bias tool (RoB 2.0). *The methods for the meta-analysis are transparent, reproducible, and follow best practice recommendations. The results of the meta-analysis are more comprehensive, considering*

Publication	Study Design	N	Safety Conclusions	Efficacy Conclusions
				multiple time points and the influence of missing data, and therefore provide more certainty on the effect of SCS in reduction of pain intensity and improvement in HRQoL.
Xu L, et al. 2022 (62)	Review of all non-pharmacologic treatment options for DPN; PRISMA guided literature search.	15 articles on the use of SCS for pain management in DPN reviewed in a qualitative analysis	Early studies reported higher infection rates after SCS in diabetic patients than the general population. But diabetes does not independently increase the rate of infection in patients receiving SCS. Root cause of increased infections not evaluated in most studies, so for the time being general guidelines to prevent surgical site infection should be strictly followed.	These studies evaluated provide moderate to strong evidence to support SCS to treat refractory DPN in the lower extremities (evidence level: 1B+). However, the use of SCS for upper extremity DPN remains to be investigated.
D'Souza et al. 2022 (63)	PRISMA guided literature search and review of evidence to support neuromodulation for the treatment of DPN	21 Publications were selected including 15 for SCS	Providers need to be aware of common complications from SCS, which have yet to be elucidated in patients with DPN, such as risk for infection, meningitis, hematoma, lead migration, hardware malfunction. In the surgical setting, there is a potential association of hyperglycemia and infection risk in patients. More studies need to be conducted to elucidate this relationship.	Level I evidence supports SCS for the treatment of DPN. Level II-3 evidence is available to support switching from tonic to burst stimulation in patients as needed.
Pluijms et al. 2011 (64)	Review of 4 SCS studies in DPN	25 patients, 6 and 4 of whom had diabetes type-I and diabetes type-II respectively.	No serious SCS related complications, infections requiring antibiotics in 14%, surgical revision required in 24%	Patients achieving 50% pain relief (VAS) compared to baseline pain scores: 84% in early pain relief (trial simulation), 50% at 3 months, 52% at 6 months, 63% at 12 months, 63% in the 2.5 – 3-year range, and 57% at 7 years. Patients achieving stoppage of analgesic usage: 67% at 1 year, 47% in the 2,5-3-year range, and 29% at 7 years.

Publication	Study Design	N	Safety Conclusions	Efficacy Conclusions
Duarte et al. 2022 (65)	Review of 4 SCS studies in DPN to evaluate superiority of different stimulation frequencies	LF-SCS: 96 patients were enrolled and randomized to SCS (n = 62) or control (n = 34) treatment. HF-SCS: 216 patients were enrolled and randomized to SCS (n = 113) or control (n = 103) treatment.	Treatment-related adverse events were reported narratively, but no safety related calculations or conclusions were made. No new safety data.	There was a significantly greater reduction in pain intensity on HF-SCS compared to LF-SCS at 6 months (MD -2.07, 95% CI -3.26 to -0.87, moderate certainty). There were no significant differences at the 3-month time point between HF- and LF-SCS.
Hoelzer et al 2022 (66)	Meta-analysis that compared safety and efficacy between 2 low-frequency and 1 high frequency studies for the treatment of DPN at six months post implantation	LF-SCS: 96 patients were enrolled and randomized to SCS (n = 62) or control (n = 34) treatment. HF-SCS: 216 patients were enrolled and randomized to SCS (n = 113) or control (n = 103) treatment.	Treatment-related adverse events were reported narratively, but no safety related calculations or conclusions were made. No new safety data.	HF-SCS achieved statistically significant increases in pain reduction compared to LF-SCS ($p<0.0001$). 72.12 % of all HF-SCS patients were responders, and 54.84% of LF-SCS patients were responders ($p=0.018$). If you compare only patients that received a permanent implant, 83.33% of HF-SCS patients were responders, and 62.96% of LF-SCS patients were responders ($p=0.0072$).

4. Safety and Effectiveness Results

Safety Results

(1) Clinical practice guidelines on the perioperative care of diabetic patients

Recommendations on the perioperative care of diabetic patients were extracted from the individual publications. Seventeen (17) of 30 records indicated that the glucose level in the perioperative stages should be below 180 mg/dL. HbA1c percentages were generally recommended to be below 8%, with several guidelines recommending postponement of elective surgeries if HbA1c levels ranged from 8% to 9%. The guidelines reviewed also provided recommendations regarding blood- sugar control medication. Metformin can generally be continued on the day of surgery but should be withheld at least 48 hours prior if a patient has renal dysfunction. Sulfonylureas generally should be stopped on the day of and up to 24 hours before surgery. Insulin treatments during the perioperative phase were noted to vary significantly in methodology and are likely dependent on many factors unique to the patient's medical history and individual characteristics.

The clinical guidelines reviewed included reference to common complications for diabetic patients undergoing surgical procedures. These complications included wound infection, impaired/compromised wound healing, vascular complications/myocardial infarction, diabetic ketoacidosis (DKA), renal dysfunction and insufficiency, increased mortality and morbidity in postoperative window, immune system dysfunction, thrombosis, and hyper/hypoglycemia.

From the selected clinical guidelines, referenced articles describing incremental risks were reviewed for rates of perioperative complications as well as relative risk levels (described as Odds or Hazard Ratios) in the diabetic population. The sources were screened for similarity of populations studied as compared to SCS (elective, orthopedic or spinal surgery, etc.). A summary is provided in Table III.5. Most noted perioperative events were more likely to occur in diabetic patients with higher HbA1c levels, with odds ratios ranging from 1.17 to 6.07. Of the data sources reviewed, diabetic patients were twice as likely to have an infection with delayed wound healing possibly contributing to this risk being 6 times more likely in patients with higher HbA1c levels (Han et al, 2013) (67). Myocardial infarction was 1.5 times more likely to occur in uncontrolled diabetic patients based on a univariate analysis but did not reach significance in the multivariate analyses (Marchant et al. 2014) (68). Stroke risk was also elevated in the same cohort (Marchant et al. 2014) (68).

Additional references provided information on the risk of CSF leaks and subdural hematomas in diabetic patients. Ha et al. 2016 reported data from a non-SCS procedure (craniotomy) concluding that diabetic patients may be at higher risk of CSF leak (univariate regression model; p=0.021), though a multivariate regression model did not find a significant relation between diabetes and CSF leak (Odds Ratio = 1.82; p = 0.448) (69). The more invasive nature of a craniotomy compared to SCS lead placement limits the applicability of this concern to SCS procedures. Wang et al. 2014 reported increased incidence of subdural hematoma in diabetic patients (log-rank test, p<0.0001) (70). This analysis considered all causes of subdural hematoma, including traumatic and non-traumatic events. Cox proportional hazard modeling resulted in an adjusted Hazard Ratio = 1.63.

In addition, as explanations for this increase in relative risk, the authors hypothesized that the prevalence of cardiovascular disease and subsequent use of anti-coagulants as well as renal disease may contribute to increases in bleeding tendency or that brain atrophy and subsequent stretching of bridging veins increases the likelihood of vessel tearing.

Table III.5. Perioperative complications and relative risk in diabetic patients.

Generalized Events	Observed Rate in Diabetic Population (source intervention, rate)	Relative Risk for Diabetic Population
Delayed wound healing	Han et al. (2013) (67): Total Knee Arthroplasty, Wound complication rate = 6.6%	Han et al. (2013): OR HbA1c > 8 = 6.07
Infection: surgical site, systemic, pneumonia	Golden et al. (1999) (71): Coronary artery surgery, Infection rate = 24.3% (SSI Leg = 10.9%, SSI sternum = 5.6%)	Golden et al. (1999): progressive trend with blood glucose and OR for infection. OR mean blood glucose (MBG) 207-229 mg/dL= 1.17; 230-252 mg/dL = 1.86; 253-353 mg/dL = 1.72
	Browne et al. (2007) (72): Lumbar fusion surgery, Infection rate = 0.68%	Brown et al. (2007): OR = 1.52
	Anderson et al. (2017) (73): Spine surgery, Infection rate for highest risk groups undergoing laminectomy = 2.3%	Anderson et al. (2017): OR = 2.04
	Marchant et al. (2009) (68): Total Joint Arthroplasty, Infection rate = 0.38% in controlled diabetes and 1.18% in uncontrolled diabetes	Marchant et al. (2009): OR = 2.28
	Wang et al. (2020) (74): Cardiac surgery, Infection rate = 2.7%	Wang et al (2020): strong association between surgical site infection rate and higher preoperative HbA1c levels in diabetic patients after cardiac surgery OR = 2.94
	Cancienne et al. (2017) (75): Lumbar decompression, Infection rate = 0.5%-3.5%	Cancienne et al. (2017): for diabetic patients with HbA1c levels ≥ 7.5% OR = 2.9
Cardiovascular events: stroke, deep vein thrombosis (DVT), myocardial infarction (MI), hemodynamic instability	Marchant et al. (2009) (68): Total Joint Arthroplasty, Myocardial infarction = 0.01%, Stroke = 0.2%	Marchant et al. (2009): Myocardial infarction OR = 1.54 in uncontrolled diabetics (p>0.05); Stroke OR = 3.42
CSF leak-subdural hematoma	Wang et al (2014) (70): Cardiac Surgery, All cause, rate of subdural hematoma in diabetic population = 2.04/1000 person years.	Wang et al (2014): Adjusted hazard ratio of 1.63 for diabetic patients for subdural hematoma.
	Ha et al. (2016) (69): Craniotomy, Rates not specific to diabetic patients	Ha et al (2016): OR = 1.82 for CSF leak in diabetic patients.

Data on diabetic and specifically DPN patients treated with SCS is included in the following sections. The safety profile of SCS used in diabetic populations appears to be similar to what is observed in non-diabetic patients in most reports, with some exceptions. The similarity in safety profile does not eliminate the fact that diabetic patients are at increased risks for perioperative complications based on broader data collection on similar elective procedures. To address the incremental risks and avoid complications in diabetic patients, safety information in device labeling has been supplemented to include additional warnings and adverse event listings. Additional information includes warnings of the potential for increased frequency or severity of events as well as selecting and managing patients presenting with risk factors or sub-optimal glycemic control. The included recommendations are in line with the most recent American Diabetes Association standards of care on diabetic patients in the hospital setting (1).

(2) Evoke System Clinical Study Safety Data

Available data on all 434 subjects enrolled in the Evoke and ECAP IDE studies of the Evoke System were included in the safety analysis; 87 subjects were diabetic and 347 non-diabetics. Adverse events adjudicated by the independent Clinical Events Committee (CEC) as possibly or definitely related to the procedure, device and/or stimulation therapy (i.e., 'related adverse events') occurring from the time of the trial procedure through up to 24-months (ECAP study) and 36-months (Evoke study) post-permanent implant were evaluated. The diabetic subjects had a mean of 21.5 months of device exposure, ranging from 1 to 2012 days.

A total of 14 related AEs occurred in 12 (13.8%) diabetic subjects. The results indicate a low incidence of related adverse events in diabetic patients with SCS, including incidence rates for the following common adverse events: 5.7% for lead migration, 2.3% for device site swelling or pain, 1.1% for hematoma, 1.1% for infection. There were no reports of CSF leak/dural tear, lead failure, or 0 uncomfortable stimulation/stimulation issues in the diabetic subjects (Table III.6). Furthermore, there was no statistical evidence of a difference between diabetic and non-diabetic subjects in the incidence of related adverse events (all $p \geq 0.20$). There was also no statistical evidence that the incidence of subsequent surgical procedures (i.e., revision, replacement, or explant) significantly differed between diabetic and non-diabetic subjects (all $p > 0.18$).

Additionally, Kaplan-Meier survival (freedom from event) analyses were performed comparing common related adverse events and subsequent surgical interventions between the diabetic and non-diabetic subjects enrolled in these studies. Infection, lead migration, lead failure, device site swelling or pain, hematoma, wound dehiscence, CSF leak/dural tear, uncomfortable stimulation/stimulation issues, revision, replacement, and explant were compared. The time course of events was generally similar (i.e., no significant differences) for diabetic and non-diabetic subjects.

These results, taken together, suggest that the use of the Evoke System in the diabetic patient population does not lead to increased risk of device related adverse events or subsequent surgical procedures.

(3) Published Literature – Safety

(a) Common Adverse Events

Studies which included detailed adverse event information were pooled to assess common adverse event occurrences. Table III.6 presents study data grouped by reports of common patient cohorts and by populations defined specifically by DPN or by those reporting on patients with diabetes in general (DM).

Table III.6. Common Adverse Events

Study		Sample Size[t,i]	Adverse Event Counts (%)						
			Infection	**Lead migration**	**Lead failure**	**Device site swelling or pain**	**Hematoma / Erosion / Wound Dehiscence**	**CSF Leak/ Dural tear**	**Uncomfortable stimulation / stimulation issues**
DPN	Petersen (2021, 2022, 2022)	104	8 (7.7)	1 (1.0)		2 (1.9)[c]	4 (3.8)		1 (1.0)
	Pluijms (2012) Slangen (2013, 2014) van Beek (2015, 2018) Zuidema (2022)	49	2 (4.1)	5 (10.2)	4 (8.2)	10 (20.4)		1 (2.0)[g]	9 (18.4)
	Galan (2020)	9				1 (11.1)[d]	1 (11.1)		
	de Vos (2014)	40	3 (7.5)[b]	1 (2.5)		2 (5)			2 (5)
	de Vos (2009)	11	1 (9.1)		2 (18.2)				
	Tesfaye (1996) Daousi (2005)	10	2 (20)	2 (20)	1 (10)		1(10)		
DM	Falowski (2019)	1663	59 (3.5)						
	Hoelzer (2017)	452	9 (2.0)						
	Mekhail (2011)	56	5 (8.9)						
	Petrakis (1999)	64	2 (3.1)	2 (3.1)					
Evoke System Clinical Studies[a]		87	1 (1.1)	5 (5.7)	0 (0.0)	2 (2.3)[e]	1 (1.1)[f]	0 (0.0)	0 (0.0)
Range			1.1%-20%	1.0%-20%	8.2%-18.2%	1.9%-20.4%	1.1%-11.1%	2.0%	1.0%-18.4%

*Studies that did not include AE information specific to the diabetic or DPN population were not included in this table.

DPN: Diabetic peripheral neuropathy; **DM**: Diabetes mellitus

t,i: Sample sizes reflect subjects exposed to either the trial stimulation or permanent IPG implant as described in the individual publications.

a: There were no reports of lead failure (i.e., lead breakage/fracture), CSF leak/dural tear, or uncomfortable stimulation/stimulation issues (i.e., overstimulation or unwanted stimulation location) in any of the diabetic patients enrolled in the IDE clinical studies of the Evoke System.

b: Two patients with infection also had fluctuations in their blood glucose levels.

c: IPG pain leading to location revision surgery

d: Based on report of implant site seroma

e: Rate of IPG pocket pain

f: Rate of hematoma; there were no reports of erosion or wound dehiscence in any of the diabetic patients enrolled in the IDE clinical studies of the Evoke System.
g: CSF leak reported in one subject during aborted trial lead placement and reported in Slangen (2014)

Published literature describing SCS to treat DPN and published clinical practice guidelines on peri-operative care of diabetic patients provides information on specific inherent risks which may be of concern for diabetic patients when it comes to the delivery and management of SCS therapy.

- **Infection**

  Data on device or procedure related infections in DPN and diabetic patients indicate a rate ranging from 1.1 to 20%. The incidence of infection in DPN and diabetic patients is comparable to overall rates of infection associated with SCS of 4.89% (range: 2.5 to 10%) as reported in a systematic literature review by Eldabe et al. (2016) (76). The results of the clinical studies of the Evoke System indicate that the incidence of related infections in diabetic patients is 1.1%, which falls below the 2-20% incidence range reported in the literature. Additionally, related infections were not significantly different between diabetic and non-diabetic patients (wound infection p-value = 1.000; non-specific infection p-value = 0.490). This finding is consistent with the results of three large retrospective studies on SCS, which also reported no significant difference in the rate of device specific infection for patients with diabetes (35,47,48). Therefore, the various sources of evidence are consistent and show DPN and diabetic patients in general do not have a higher risk of device/procedure related infections. The data also suggests that diabetic patients have an increased risk of all cause infection; however, this risk can be appropriately communicated through device labeling and clinical guidelines.

  Infections were either resolved using solely antibiotics or through removal of the infected components of the SCS system followed by administration of antibiotics.

  The only complications as a result of infections explicitly mentioned in the literature include device explant, abscess formation, and changes in glucose level stability. Specifically, Peterson et al. (2022) reported that out of eight patients who had procedure- related infections, three were able to resolve the infection with conservative treatments with no specified complications, whereas five required surgical explant of the device (52). Another infection related complication is an increased risk of blood glucose fluctuations. This risk is highlighted by de Vos et al. (2014) in which two subjects experienced fluctuations in blood glucose levels in response to an infection (44). Although the study did not attribute these infections to the device, the impact of blood glucose fluctuations in diabetic patients that may arise from device-related infections can lead to increased morbidity and mortality in this patient population. Of note, the one infection that occurred in the clinical studies of the Evoke system did not result in device explant, abscess formation, or changes in glucose level stability that were noted.

- **Wound Healing Complications Including Hematoma, Erosion, Wound Dehiscence**

  Data on adverse events related to wound healing such as hematoma, erosion, and wound dehiscence in DPN and diabetic patients indicate a rate ranging from 1.1 to 11.1%. The results of the clinical studies of the Evoke System indicate that the incidence of hematoma, erosion, or wound dehiscence in diabetic patients is 1.1% (one report of hematoma; no reports of erosion or wound dehiscence in diabetic patients), which falls below the 3.8-11.1% incidence range reported in the literature. Additionally, the rates of

hematoma, erosion, or wound dehiscence were not significantly different between diabetic and non-diabetic patients (hematoma p-value = 0.490; wound dehiscence p-value 0.588; no reports of erosion in diabetic or non-diabetic patients).

Diabetes is known to be a potential risk factor for wound healing (e.g., hematoma, erosion and wound dehiscence), which can lead to infection. However, rates of these events may be underreported due to subsequent development of a more serious adverse event such as infection.

- **Cardiovascular events**

  Reports of subject or patient death attributed to myocardial infarction (n=3) or cardiac arrest (n=1) were reported in the published literature on SCS to treat DPN (44,56). However, none were reported to be related to SCS procedures or therapy, though patients with poorly controlled diabetes may have an elevated risk for cardiovascular events in the perioperative period. In an analysis of outcomes in patients undergoing elective orthopedic surgery (Marchant et al, 2009), patients with poor glycemic control showed a non-significant trend towards greater odds of myocardial infarction and a significantly greater odds of stroke (odds ratio 3.42 CI: 1.87-6.25; $p < 0.001$) (68). There were no deaths due to a cardiac event in diabetic patients enrolled in the clinical studies of the Evoke System.

- **Dural puncture and CSF leak**

  Slangen et al. (2014) reported one death due to subdural hematoma after dural puncture during the attempted trial lead implantation (39). A review of the literature was conducted to identify publications that report CSF leak in patients with diabetes. Data from craniotomy procedures in Ha et al. (2016) and Hutter et al. (2014) suggest that diabetes may be a risk factor for CSF leaks (69,77). However, the more invasive nature of craniotomy procedures limits the generalizability of this concern to SCS procedures. Wang et al. (2014) also reported a 1.57-fold higher incidence of subdural hematoma in diabetic patients than in non-diabetic patients (2.04 vs. 1.30 per 1000 person-years), with an adjusted hazard ratio of 1.63 [95% confidence interval (CI) 1.43–1.85] (70). There were no reports of dural puncture or CSF leak in diabetic patients enrolled in the clinical studies of the Evoke System.

- **Glycemic control**

  de Vos et al (2014) reported 2 subjects experiencing fluctuations in blood glucose levels following infections (44). While these were determined by authors to be unrelated to SCS, the physiologic stress of surgery or any adverse event may impact glycemic control.

- **Mortality and morbidity: Patient deaths and other serious adverse events**

  TenVaarwerk et al. (1999) published a multi-center retrospectives study characterizing the morbidity and mortality of patients treated with SCS for refractory Angina Pectoris (32). The study included 517 subjects treated with SCS between 1987 and 1997, 14% of which were identified as having insulin dependent Diabetes Mellitus (IDDM). A multi-variate analysis significantly correlated IDDM with mortality (p =0.01). However, the

health status of the population in this report limits the generalizability of this data to a broader population of DPN patients, especially to those patients without severe cardiovascular complications. Specifically, before spinal cord stimulation, 66% of the patients of the patients included in this study had experienced myocardial infarction, 68% of them had three vessel disease and in 24% the left ventricular ejection fraction (LVEF) was ≤40 %. Moreover, angioplasty and bypass surgery were performed in 17% and 58% of the subjects, respectively.

As discussed above, Tesfaye et al. (1996) and Daousi et al. (2005) reported 3 deaths over the 7-year study period (31,56). These deaths occurred at 2 months, 2 years, and 4 years after implantation and were all attributed to myocardial infarction. All three subjects had reported continuous pain relief from regular use of their SCS until the time of their death.

de Vos et al. (2009) reported one death out of the 11 patients who enrolled in the study. The authors noted that the cause of death was unrelated to SCS (34).

de Vos et al. (2014) reported one case of prolonged hospitalization due to coagulopathy following the implant procedure (44). As discussed above, the publication also described one subject in the SCS group that experienced cardiac arrest unrelated to the study procedure.

As discussed above, Slangen et al. (2014) reported one death out of 22 patients assigned to the SCS treatment group due to dural puncture during implantation of the trial stimulation lead (39). The dural puncture led to a subdural hematoma over the left hemisphere and a midline shift and the patient died 10 days after the surgery.

One death due to kidney failure occurred in a patient enrolled in the clinical studies of the Evoke System who had a baseline history of diabetes and renal insufficiency. The event was determined to be unrelated to the SCS procedure, device, or stimulation therapy.

- **SCS-specific events**

  Device events may be associated with or the cause of certain adverse events. Several reports describe hardware-specific complication rates including SCS system survival, lead migration, and lead failure.

  - **SCS system survival**

    Bir et al. (2016) reported the rates of overall system survival for 141 patients treated at a single center and compared the diabetic population relative to the non-diabetic population (45). System survival was defined as being free from revision for any reason including device failure, migration, infection, or loss of effect. The revision-free survival time was 35 months for the diabetic population and 43 months for the non-diabetic population. The authors reported no statistical difference between the revision free survival time (log rank p = 0.98). Antonovich et al. (2021) conducted a retrospective review of patients treated with SCS for chronic pain and found diabetes was not associated with reoperation (p = 0.197) (50). Of note, the rate of device revision, replacement, or explant was not significantly different between diabetic and non-diabetic

patients enrolled in the clinical studies of the Evoke System (revision p-value = 0.304; replacement p-value = 0.319; explant p-value = 1.000).

- **Lead migration**

  Data on lead migrations in DPN and diabetic patients indicate a rate ranging from 1-20%. The incidence of lead migration in DPN and diabetic patients is comparable to overall rates of lead migration associated with SCS of 15.49% (range: 2.1 to 27%) as reported in a systematic literature review by Eldabe et al. (2016) (76). The results of the clinical studies of the Evoke System indicate that the incidence of lead migration in diabetic patients is 5.7%, which falls within the 1-20% incidence range reported in the literature. Additionally, lead migrations were not significantly different between diabetic and non-diabetic patients (p-value = 0.353).

- **Lead failure**

  Data on lead failure, including lead fracture/breakage or malfunction, in DPN and diabetic patients indicate a rate ranging from 8.2%-18.2%. The incidence of lead failure in DPN and diabetic patients is comparable to overall rates of lead failure associated with SCS of 6.37% (range: 0 to 10.2%) as reported in a systematic literature review by Eldabe et al. (2016) (76). The were no reports of lead failure in diabetic patients enrolled in the clinical studies of the Evoke System.

Effectiveness Results

(4) Published Literature – Effectiveness

The evaluation of the effectiveness of the Evoke System was conducted via a systematic review of published clinical studies that evaluated the effectiveness of legally marketed, fully implantable SCS systems in treating chronic, intractable pain in the trunk and/or limbs, and diabetic peripheral neuropathy of the lower extremities. The literature search identified 15 publications from 8 studies reporting results applicable to evaluate the effectiveness of SCS for DPN (Table III.3).

(a) Non-comparative studies

Eleven (11) publications include data from 6 single-arm studies that evaluated the use of SCS to treat DPN (31,33,34,36–38,41–43,56,58). SCS trial success rates ranged from 73% to 93%. The proportion of subjects assessed as successfully treated ranged from 55% to 100% with average pain relief ranging from 41% to 80% (up to 12 months). Successful treatment during long term follow-up ranged from 40% to 77% (24 months to 10 years).

(b) Comparative studies

Two (2) randomized controlled trials (RCT) investigated the use of SCS to treat DPN; results from these studies were described in 6 publications (39–42,44,57). Table III.7 presents a comparison of the two initial studies which reported on the primary outcomes.

Table III.7. Details of publications describing randomized studies on DPN

Publication	**Slangen et al. 2014** (39)	**de Vos et al. 2014** (44)
Sponsor	Maastricht University Medical Center (NCT01162993)	Medisch Spectrum Twente (ISRCTN03269533)
Population	Diabetes patients with moderate to severe DPN in the lower limbs who were refractory to conventional medical treatments for more than 12 months NPRS pain rating ≥ 5 Between 18 and 80 years of age	Patients with DPN in the lower extremities for more than 1 year and refractory to conventional treatments VAS pain rating ≥ 50 mm ≥ 18 years of age
Design-allocation	Open Label, Randomized, Parallel assignment (3:2)	Open Label, Randomized, Parallel assignment (2:1)
Comparator	Best medical treatment (BMT)	Best conventional medical practice (BCMP)
Sample size (countries)	36 from 2 centers (NL)	60 from 7 centers (NL, BE, DK, DE)
Primary endpoint	≥ 50% pain reduction during daytime or nighttime or a score of ≥ 6 on a 7-point Likert scale of the PGIC for pain and sleep	Treatment success at 6 months, ≥ 50% pain reduction
Publication date	Nov 2014	Nov 2014

The demographic characteristics of subjects in both studies were similar for age, duration of disease (diabetes and DPN), and gender. Fewer Type I diabetic subjects were included in Slangen et al. However, in both studies the majority of subjects were diagnosed as Type II diabetics. Subject demographics for each study are presented in Table III.8.

Table III.8. Comparison of study demographics

Demographic[a]	**Slangen et al.**	**de Vos et al.**
Age (years)	56.9	59.0
Duration of diabetes mellitus (years)	12.7	16.3
Duration of Pain (years)	5.5	7.0
Male	67%	63%
Female	33%	37%
Type I	11%	25%
Type II	89%	75%

[a]Data are pooled for the SCS and Control groups and reported as weighted averages within each study.

Primary pain-related outcome measures between the two trials were compared to determine if the trials demonstrated similar effectiveness levels within the two similar populations; the subject measure averages are shown in Table III.9. Pain-related outcomes were similar between studies with slightly greater reductions in pain reported by de Vos et al. Control groups from

both studies did not achieve any notable reduction in average pain; however, one subject in the control arm reported treatment success.

Table III.9. Comparison of pain measures (95% CI)

Pain ratinga	Slangen et al.		de Vos et al.	
	SCS (n=22)	Control (n=14)	SCS (n=40)	Control (n=20)
Baseline	7.1 (6.3-7.9)	6.5 (5.5-7.5)	7.3 (6.8-7.8)	6.7 (5.9-7.5)
6-month	4[d] (2.6-5.4)	6.5 (5.4-7.6)	3.1 (2.2-4.0)	6.7 (5.7-7.7)
Pain reliefb	44%	0%	58%	0%
Responder Ratec	59% (36%-79%)	7% (0%-34%)	63% (46%-77%)	5% (0%-25%)

[a] VAS (0-100 mm) and NRS (0-10) were normalized to a 0-10 scale
[b] 95% CI not provided due to required distributional assumptions
[c] Study design defined successful pain relief by different measures
[d] n=19 subjects with available data for pain scores at 6-months

Combined data from comparative studies

Because the two RCTs had highly similar trial designs and patient populations and both compared SCS to standard-of-care with primary endpoints at 6 months, data from both studies were pooled and are presented in Table III.10. Average values were weighted by the number of subjects in the respective SCS and Control treatment groups for each study.

Table III.10. Combined subject measures (95% CI)

Measure	SCS (n=62)	Control (n=34)
Age (years)	57.7	59.1
Duration of DM (years)	14.8	15.2
Duration of Pain (years)	6.6	6.1
Male	65%	65%
Female	35%	35%
Type I	21%	18%
Type II	79%	82%
Average Baseline pain rating	7.2	6.6
Average 6-month pain rating	3.4	6.6
Average Pain reductiona	53%	0%
Responder Rate per protocol b,c	61% (48%-73%)	6% (0%-20%)
Responder Rate ≥ 50% reduction in painc	55% (42%-68%)	3% (0%-15%)
Responder Rate per protocol as-treatedd	70% (56%-82%)	6% (0%-20%)
Responder rate ≥ 50% reduction in pain as-treatedd	63% (49%-76%)	3% (0%-15%)

[a] Confidence interval for the percent mean change have not been calculated because biased due to the percent asymmetry
[b] Each study design defined successful pain relief by different measures
[c] Analysis of all randomized subjects in an intent-to-treat approach
[d] Including only subjects who received an SCS system implant

Meta-analysis for comparative studies

A meta-analysis of the Responder Rate (≥ 50% pain relief) from the two RCTs was performed. A random effects analysis of heterogeneity between studies supported homogenization (Cochran's Q = 0.113, p-value = 0.737; Higgin's I^2 test = 0.0%). The confidence intervals of these

studies overlap and the estimate of odds ratios are consistent, demonstrating subjects treated with SCS for DPN are more likely to achieve ≥ 50% pain relief at 6 months compared to standard-of-care. The overall mean log OR is 3.21 (95% CI 1.68 to 4.73), corresponding to an Odds Ratio of 24.8 in favor of treatment success with SCS for the treatment of DPN.

A second analysis based on fixed effects model on the risk differences was performed. Similar to the random effects analysis, there is not statistically reliable evidence of heterogeneity between the studies I^2= 0.0%, and Q = 0.129 (p= 0.719). The fixed effect model estimates a group difference of 55.3% with a 95% CI from 40.8% to 69.9% (see Table III.11). The data pooled from both studies showed that the binomial responder rates (defined as ≥ 50% reduction in pain at 6-months) for all subjects randomized to receive SCS treatment was 62.9% and supports probability of treatment success.

Table III.11. Fixed Effects Results for 50% Responder Rates

Measure	SCS (N= 62)	Control (N= 34)	Difference
Responder rate ≥ 50% reduction in pain as-treated	62.9% (49.7% - 74.8%) [1]	5.9% (0% - 19.7%) [2]	55.3% (40.8% - 69.8%) [3]
[1] Binomial interval calculated with x = 39 and n = 62.			
[2] Binomial interval calculated with x = 2 and n = 34.			
[3] Interval from Fixed Effect Meta Analysis shown above.			

Long-term effectiveness

van Beek et al (2018) (41) published long-term follow-up results for subjects from the studies reported by Pluijms et al (2012) (36) and Slangen et al (2014) (39). Forty-eight subjects (40 with permanent implant) were included in the analysis for follow-up to 5 years. Treatment success was defined as ≥ 50% pain relief in day or nighttime pain or a PGIC rating of "much improved" or "very much improved". Treatment success was observed in 86%, 71%, 77%, 67%, and 55% at 1 (n = 36), 2 (n = 35), 3 (n = 34), 4 (n = 30), and 5 (n = 22) years, respectively. A Michigan Diabetic Neuropathy Score (0 to 3 scale) of 3 at baseline was associated with treatment failure during the 5-year follow-up (hazard ratio 3.9; p-value = 0.014). This suggests patients with severe neuropathy may be less likely to experience treatment success.

Zuidema et al (2022) published the results on the 19 subjects from this same cohort who had ≥8 (range 8-10) years follow-up (42). The authors observed that the efficacy stabilized after 5 years with consistent results out to 8-10 years follow-up.

Pediatric Extrapolation

We believe that existing clinical data can be leveraged to support a reasonable assurance of safety and effectiveness of the subject device in a pediatric sub-population of adolescents aged 18-21.

In accordance with section 515A of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), an analysis was conducted on the available information about pediatric subpopulations who suffer from chronic, intractable pain of the trunk and/or limbs. The pediatric population is defined as patients 21 years of age or younger. While FDA considers patients aged 18-21 to still be pediatric in nature, this is a population that requires no special considerations and is treated the same as an adult population 22 years of age and older (“Transitional adolescent B”). The

discussion below follows the decision tree in the FDA Guidance Document "Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices", issued June 2016.

Diabetic peripheral neuropathy is a condition that can occur in individuals who are 18-21 years of age. Jaiswal et al (2017) assessed the prevalence of DPN in pediatric populations with either type 1 or type 2 diabetes enrolled in a clinical study (78). Prevalence of DPN in pediatric patients with type 1 diabetes was found to be 7%, and 22% for pediatric patients with type 2 diabetes. This particular study enrolled 1,734 patients with type 1 compared to 258 with type 2 diabetes. The mean age of the type 1 diabetes patients was 18 ± 4 years, with a duration since diagnosis of 7.2 ± 1.2 years. Within the type 2 population, the mean age was 22 ± 3.5 years, with a duration since diagnosis of 7.9 ± 2 years. To the best of our knowledge, there is no requirement that the prevalence meets or exceeds a certain percentage to qualify for extrapolation.

There are endpoints present in the existing data sources that measure the device effects relevant to the intended pediatric population. The types of endpoints measured in adult populations are the same as those that would be used in pediatric subpopulations. These include the visual analog scale (VAS), numerical rating scale (NRS), among others. Clinical studies often consider adults to be 18 years of age and older, and there are no special considerations for the 18-21 age range with respect to the assessment of safety or efficacy outcomes. Published articles such as one by Moser et al (2017)[129] evaluating the development of a "youth-report measure of DPN symptoms" focuses on patients under 17, which we are not including for consideration here (79).

The Evoke System is implanted and there are no differences between the adult and pediatric populations in the location or duration of implantation that could affect safety or effectiveness in a clinically meaningful way. The positioning of the device is the same for adults aged 22 and older as would be for patients aged 18-21. There is no need for specific instructions related to the implantation of the device for the 18-21 age range relative to the older than 22 years population. Therefore, there are no differences in the location or duration of implantation that could affect the safety or effectiveness of the device in a clinically meaningful way.

Additionally, there are no differences in device characteristics between pediatric and adult use that could affect safety or effectiveness in a clinically meaningful way. The Evoke System needs no modifications to be used for a patient aged 18-21 compared to those patients aged 22 and older. Both adults aged 22 and older and patients aged 18-21 will use the same hardware, with the specific hardware selections being individualized according to the particular needs of the patient, as is done currently. Similarly, the stimulation is set on an individual basis, and is not calibrated any differently for the 18-21 years of age subpopulation. Therefore, there are no differences in device characteristics that could affect the safety or effectiveness of the device in a clinically meaningful way.

There are no unique characteristics of the device that could affect safety or effectiveness in a clinically meaningful way when used in the pediatric population. As mentioned above, the type of population to which we seek to extrapolate data includes transitional adolescents who are treated like adults. In that regard, there is no evidence to suggest that there are substantial differences between patients who are 18-21 years of age with DPN and those who are aged 22 and older with DPN. Skeletal maturity is achieved by age 18, for example, and relative to a

patient who is 22 years of age, any group differences are negligible. Therefore, there are no characteristics that are unique to the intended pediatric subpopulation that could affect the safety or effectiveness of the device in a clinically meaningful way.

There are no differences in the disease characteristics between pediatric and adult populations that could affect safety or effectiveness in a clinically meaningful way. While there may be differences in risk factors for the development of DPN, that is not important to the discussion either of extrapolation specifically or safety and effectiveness in general because the system is not intended for use in diagnosis of DPN – patients who will use the Evoke System will have previously been diagnosed with DPN, the process of which is the same for adults aged 22 and older as it is for patients who may be aged 18-21. With respect to the disease itself, we are not aware of any evidence to suggest an age-related difference in the clinical symptoms of DPN, such that the presentation of DPN symptoms in an 18-year-old could be said to be different from those of a 22-year old in a clinically meaningful way. Therefore, there are no differences in disease characteristics that could affect the safety or effectiveness of the device in a clinically meaningful way.

As described above, we are not aware of any evidence to suggest there are age-related differences in the characteristics of the disease, nor are we aware of any unique characteristics between the intended 18-21 years of age pediatric population and the adult population aged 22 and older. We are similarly not aware of any additional differences between the adult and pediatric populations that could affect the safety or effectiveness of the Evoke System for the treatment of DPN in a clinically meaningful way.

Having established that the adult and intended pediatric subpopulations are sufficiently similar, the next question to be addressed is whether the adult data are of sufficient quality to permit extrapolation. It is our position that the data are in fact of sufficient quality to permit extrapolation.

The body of evidence described in this submission includes data from a significant number of study subjects and patients, and the studies that were analyzed have been peer-reviewed for publication. As will be described in the benefit-risk analysis section below, there is a reasonable amount of certainty present with respect to the evidence both for safety as well as effectiveness. If the evidence is sufficient to support a determination of a reasonable assurance of safety and effectiveness, it is also sufficient for the purposes of pediatric extrapolation. Therefore, we believe it is appropriate to extrapolate the adult data where SCS is used to treat DPN to the population aged 18-21.

III.B. Conclusions Drawn from Preclinical and Clinical Studies

1. Effectiveness Conclusions

A total of 15 publications from 8 studies (several publications reported alternative analyses or long-term follow-up) described effectiveness outcomes associated with SCS to treat DPN. Two RCTs comparing SCS to the standard-of-care included a total of 96 subjects, four prospective studies without a comparator included a total of 84 subjects, and two retrospective studies contained data on 68 patients with diabetic neuropathy.

Two independent RCTs evaluating SCS to treat DPN compared to standard-of-care included a total of 62 subjects in the treatment group and 34 subjects in the control group. At the 6-month primary endpoint, the outcomes for subjects randomized to receive SCS treatment were consistent between both studies with treatment success rates of 59% and 63% and an average pain relief of 44% and 58% for Slangen et al (2014) and de Vos et al (2014), respectively.

The data pooled from both studies showed that the binomial responder rates (defined as ≥ 50% reduction in pain at 6-months) for all subjects randomized to receive SCS treatment was 62.9% and supports probability of treatment success. A meta-analysis of both studies resulted in an overall mean log OR of 3.21 (95% CI 1.68 to 4.73), corresponding to an Odds Ratio of 24.8 in favor of treatment success with SCS for the treatment of DPN.

Long-term efficacy data on subjects treated with SCS to treat DPN from one nonrandomized study and one RCT reflecting outcomes after 8-10 years of treatment showed a sustained pain relief at clinically meaningful levels.

There were an additional 8 meta-analyses that independently reviewed effectiveness from previously published studies and determined that there was sufficiently strong evidence to support the use of SCS to treat DPN.

The data from all these studies support the effectiveness of the Evoke System for treating patients who suffer from chronic, intractable pain of the trunk and/or limbs, including diabetic peripheral neuropathy of the lower extremities.

2. Safety Conclusions

The clinical evidence supporting the safety of the Evoke System to treat DPN includes a systematic literature review of published scientific literature reporting SCS to treat chronic intractable pain in patients with diabetes in general, and data from diabetic patients enrolled in IDE clinical studies of the Evoke System. Safety data from 223 subjects across 6 studies treated with SCS for their DPN were included. An additional 2322 patients were included across 6 studies which reported on diabetic patients treated with SCS. The rates of common adverse events in the DPN population were similar to that of the general SCS population. The published literature on SCS to treat DPN and the published clinical practice guidelines on perioperative care of diabetic patients described some inherent risks for diabetic patients treated with SCS including, but not limited to, infection, delayed wound healing, cardiovascular events, dural puncture and subsequent subdural hematoma, and fluctuations in glycemic control. These events can be mitigated through appropriate patient selection, and/or by the use of appropriate surgical techniques and procedures and have been included in the labeling.

There were an additional 8 meta-analyses that independently reviewed safety information and determined that risks of SCS in the diabetic population were similar to the conclusions from the previously published studies.

Refer to the labeling for safety information and considerations specifically addressing the use of the Evoke System in the diabetic population.

3. Benefit-Risk Determination

Diabetic peripheral neuropathy is nerve damage caused by chronically high blood sugar and diabetes. It leads to numbness, loss of sensation, and sometimes pain in the feet, legs, or hands. It is the most common complication of diabetes.

About 60% to 70% of all people with diabetes eventually develop peripheral neuropathy. Beyond management of glycemic control, only palliative treatments are available. The best way to prevent or manage DPN is to keep the patient's blood sugar within the target range. If the patient develops DPN, the primary treatments are for pain relief. Currently, medications such as anticonvulsants, antidepressants, and opioids are approved by the FDA for the treatment of diabetic neuropathy. Non-pharmacologic treatments (physical therapy, cognitive therapy, and transcutaneous electrical nerve stimulation [TENS]) should be provided in conjunction with first-line medical treatment. Often times, however, these options are no longer effective, and the patient needs other solutions to treat their DPN. Given the considerable and growing population with diabetes, a significant number of people likely remain undertreated and without alternatives for relief.

The primary benefit of the Evoke System is the improvement in pain, including for diabetic peripheral neuropathy. SCS has been utilized for decades to treat a number of pain etiologies, and continues to provide clinical benefit for a number of different indications. SCS for the treatment of diabetic peripheral neuropathy is no different and the literature has shown that SCS can greatly improve the patient's pain, quality of life, and even reduce their analgesic and opioid use.

Studies have shown the short- and sustained long-term benefit of SCS to treat DPN both through pain relief and quality of life improvements. Pain relief is reduced on average over 60% with SCS. The improvement in pain relief is often accompanied by improvement in quality of life, which was observed in several studies. These two endpoints demonstrate that once SCS is used to treat DPN, the patient may return to a pain-free normal quality of life, without increased medication usage.

The two main sources of uncertainty that are associated with the evidence to support benefit are the influence of confounding factors such as medications and the variability of the study designs included in the systematic review. With respect to medication usage, there is no evidence to suggest that there is any difference in the influence of medication usage for a DPN population compared to other pain etiologies for which SCS is approved. These patients will generally continue to remain on at least some medications, and perhaps the best indicator that the influence of those treatments is minimal is that in general, patients treated with SCS tend to decrease their overall medication intake rather than increase it. With regard to the nature of the systematic review, there is expected to be some variability in the study designs, as they have been conducted by a number of different organizations for a variety of purposes. However, the combined evidence from these studies describes a consistent patient population, and consistently describes the clinical benefits that are experienced. Additionally, the random and fixed effects analyses supported homogenization of the RCTs that demonstrated superiority of SCS versus standard-of-care to treat DPN.

An assessment of the published literature on SCS to treat DPN provided information on the specific inherent risks for diabetic patients in the delivery and management of SCS therapy. This

included 2545 patients across 12 studies which reported on safety and adverse events in an identifiable diabetic population. The analysis of the adverse event profile of SCS to treat DPN showed common adverse event rates were within the ranges reported for the general population of SCS patients, with two notable differences: infection and the potential for blood glucose to fluctuate in response to an adverse event. Of note, there were no differences in the rate of infection between diabetic and non-diabetic patients enrolled in the IDE clinical studies of the Evoke System. Additional risks for diabetic patients include, but are not limited to, delayed wound healing, cardiovascular events, dural puncture and subsequent subdural hematoma. In the analysis of the Evoke System safety data for diabetic patients enrolled in the IDE clinical studies, the adverse events rates for these risks were within or lower than the range reported in the literature. These events may be avoided by appropriate patient selection, and/or by the use of appropriate surgical techniques and procedures.

For intractable pain resulting from DPN, patients have few options after medical management. No disease-modifying intervention beyond medications is available to treat DPN. In two well designed and executed randomized clinical trials comparing SCS to treat DPN to standard-of-care, most patients, as shown above, experienced clinically meaningful reduction in pain symptoms, and most did so beyond the primary endpoints of the studies. In a comprehensive review of the available data on the risks associated with the therapy, the risk profile for DPN patients was generally consistent with the overall risk profile for the general population treated with SCS, with the exceptions of infection and glycemic control. However, there has been no data to suggest that infection is associated with the use of SCS specifically for DPN. These risks may be mitigated by the addition of language in the labeling for the population of pain patients with DPN, such that these patients can be properly selected and managed, particularly in the perioperative phase. Thus, for patients who are not contraindicated, the clinical data has demonstrated that SCS offers a safe and effective treatment option for DPN where the benefits outweigh the risks associated with the therapy.

Patient Perspective

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for the Evoke System when used as an aid in the management of chronic, intractable pain of the trunk and/or limbs- including unilateral or bilateral pain associated with DPN of the lower extremities.

4. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The options that are currently available for the treatment of DPN beyond the management of a patient's glycemic control consist only of palliative treatments, which are largely pharmaceutical in nature. For intractable pain as a result of DPN, patients have few options after medical management. In two well-designed and executed randomized studies comparing SCS to treat DPN to the standard-of-care, most subjects experienced clinically meaningful reduction in pain symptoms, and most did so beyond the primary endpoints of the studies. In a

comprehensive review of available data on the risk profile of the therapy in DPN patients, the adverse event profile of the therapy was consistent with that of the general population treated with SCS overall, with the exception of an increased infection rate and exacerbation of unstable blood glucose levels if an adverse event were to be experienced. There is evidence from the literature to support the addition of language in the labeling that is specific to the population of pain patients with DPN, such that patients can be properly selected and managed particularly in the perioperative phase. Furthermore, the rate of these risks in diabetic patients with the Evoke System was found to be within, and in most cases, below the range reported in the literature. These patients have relatively few treatment alternatives, and for patients without contraindications, SCS offers an option for the treatment of intractable DPN where the benefits outweigh the risks associated with the therapy.

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Evoke® SCS System Surgical Guide

Instructions for the use and implantation of the Evoke SCS System

Rx Only

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Refer to the Evoke SCS System Clinical Manual for:

- Instructions on the use of the Evoke Clinical Interface and the Evoke Clinical System Transceiver.
- Instructions on programming the Evoke SCS System.

Refer to the Evoke SCS System User Manual for:

- Instructions on the use of the Evoke Patient Controller (EPC) and Evoke Charger.

Refer to the Evoke SCS System MRI Guidelines for information on the safe use of the Evoke System in an MRI environment.

Manuals are accessible at https://www.saludamedical.com/manuals.

1 Description

The Saluda® Medical Evoke® SCS System is a Spinal Cord Stimulation (SCS) system that incorporates ECAP-controlled closed-loop stimulation for the management of chronic, intractable pain. The Evoke System measures evoked compound action potentials (ECAPs) and may be programmed to deliver either ECAP-controlled closed-loop SCS or fixed-output open-loop SCS.

The Evoke Clinical Interface (CI) and Evoke Clinical System Transceiver (CST) enable the programming of the implantable Closed-Loop Stimulator (CLS) and the non-implantable external Closed-Loop stimulator (eCLS), which deliver therapy to the spinal cord through the Evoke CAP12™ Percutaneous Leads and Lead Extensions (if used).

The Evoke System may be used in conjunction with other pain management therapies, as determined by the physician.

1.1 The concept of ECAP-controlled physiologic closed-loop SCS

The Evoke System uses ECAP amplitude to measure the patient's neural response and provide physiologic closed-loop controlled SCS. The ECAP amplitude is a measure of the spinal cord activation or number of dorsal column fibers in the spinal cord that are activated by a stimulation pulse. When closed-loop (CL) is enabled, the system automatically varies the stimulation current for every pulse to maintain consistent spinal cord activation during physiological changes and movement.

Figure 1.1, below, depicts the concept of a physiologic closed-loop controlled system using ECAPs. Following a stimulation impulse, the amplitude of the ECAP that is generated in the spinal cord by that stimulus is recorded. The ECAP amplitude is compared to the selected target and then used to automatically adjust the current of the next stimulus to maintain a consistent ECAP amplitude.

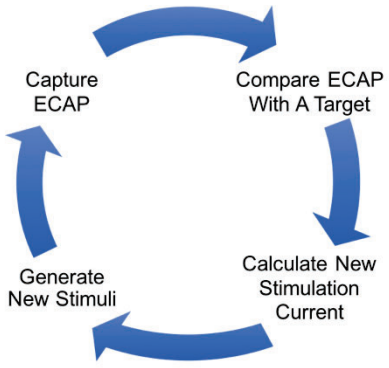


Figure 1.1: ECAP-Controlled Closed-Loop SCS.

1.2 System Components

1.2.1 Evoke Closed-Loop Stimulator (CLS)

Ref No. 3002, 3042

The Evoke Closed-Loop Stimulator (CLS) is a totally implanted spinal cord stimulator that connects to the CAP12 Percutaneous Leads and is implanted under the skin for long-term therapy. The CLS delivers either closed-loop or open-loop stimulation through the leads and measures the neural response to stimulation. A port plug is provided with the CLS, for insertion into an unused CLS port when only one lead is implanted.

1.2.2 Evoke External Closed-Loop Stimulator (eCLS)

Ref No. 3036

During the trial stimulation period, the CAP12 Percutaneous Leads are connected to the Evoke External Closed-Loop Stimulator (eCLS). The eCLS is an external stimulator used for intraoperative testing and during the trial stimulation period. The eCLS delivers either closed-loop or open-loop stimulation through the leads and measures the neural response to stimulation.

1.2.3 Evoke eCLS Case

Ref No. 3035

The Evoke eCLS Case is used by the patient to house the eCLS during the trial stimulation period. The kit also includes two lead adapters to connect the leads or lead extensions to the eCLS

1.2.4 Evoke CAP12 Percutaneous Lead Kit, 60cm and 90cm

Ref No. 3008/3016/3009/3017

The Evoke CAP12™ Percutaneous Leads are placed in the epidural space overlying the spinal cord and are connected to an eCLS for a trial stimulation period, or to a CLS for long-term therapy. One or two leads, each with 12 electrodes, are implanted. The lead kit is provided with one suture anchor to secure the lead, and surgical accessories (epidural needle and two stylets) for use during lead placement.

1.2.5 Evoke CAP12X Lead Extension Kit, 55cm

Ref No. 3011

The Evoke CAP12X™ Lead Extensions are used when trialing a permanently implanted lead, where the extension is externalized for connection to an eCLS.

1.2.6 Evoke Active Anchor Kit

Ref No. 3043

The Evoke Active Anchor allows the surgeon to secure the lead after placement in the epidural space. The active anchor kit is provided with two active anchors and a torque wrench to tighten the anchor. Kits labelled as Evoke Active Anchor Kit - L are supplied with a Long Torque Wrench.

1.2.7 Evoke Intraoperative Cable Kit

Ref No. 3034

The Evoke Intraoperative Cable allows the surgeon to connect the eCLS to the implanted leads for intra-operative testing.

1.2.8 Evoke Tunneler

Ref No. 3012

The Evoke Tunneler allows the subcutaneous threading of leads and/or lead extensions, either to an exit incision for the trial stimulation period, or to the CLS (leads only).

1.2.9 Evoke Spares Kit

Ref No. 3015

The Evoke Spares Kit contains all items from the permanent lead kits except for the lead itself, plus a CLS port plug and torque wrench. The Evoke Spares Kit will save surgeons from opening a new lead kit should any of the small accessory items be dropped or damaged during the procedure.

1.2.10 Epidural Needle 6.5”

Ref No. 3014

The 6.5” Epidural Needle Kit is an optional long needle for larger patients in whom the regular 4.5” needle supplied with the lead kits is too short to reach the epidural space.

2 Indication for use

The Saluda Medical Evoke SCS System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following:

- Failed back surgery syndrome
- Intractable low back pain and leg pain
- Diabetic peripheral neuropathy of the lower extremities

3 Contraindications

The Evoke SCS System should not be used in patients who:

- Do not receive effective pain relief during trial stimulation
- Are unable to operate the Evoke SCS System.
- Are unsuitable surgical candidates.

4 Safety information

For warnings and precautions associated with the Clinical Interface (CI), Clinical System Transceiver (CST) and associated programming, please refer to the Evoke SCS System Clarity Clinical Manual.

For full details on the safe use of the Evoke SCS System in the MRI Environment please refer to the Evoke SCS System MRI guidelines.

Manuals are accessible at https://www.saludamedical.com/manuals.

Patients must be advised of the following warnings and precautions (Sections 4.1 and 4.2).

4.1 Warnings

⚠ Diathermy

- Patients implanted with the Evoke System should not be subjected to shortwave, microwave and/or therapeutic ultrasound diathermy.
- Diathermy generates energy that may cause heating at the lead site, resulting in damage to the CLS, tissue damage, severe injury, or death.

⚠ Magnetic Resonance Imaging (MRI)

Note: Refer to the Evoke SCS System MRI Guidelines for information on the safe use of the Evoke System in MRI environment.



The Evoke System is MR Conditional in certain system configurations, under specific scanning parameters. Full details can be found in the Evoke SCS System MRI Guidelines. These instructions should be followed exactly. MRI scanning of an unapproved system configuration could lead to vibration or torque on the device and heating of the implanted system, which may cause internal tissue damage, or permanent damage to the stimulator, which may cause loss of therapy.

⚠ CT Scans

- Patients implanted with the Evoke System may experience a momentary increase in stimulation when receiving a CT scan. Some patients have described this as uncomfortable stimulation, jolting, or a shocking sensation.
- Prior to a patient undergoing a CT scan, turn the stimulator off.

⚠ Electrosurgery

- Patients implanted with the Evoke System should not be subjected to electrosurgical techniques, such as electrocautery, in close proximity to the Evoke System components.
    - Electrosurgical devices generate energy that may cause tissue damage at the lead site and result in severe injury.
    - Damage may also occur to the CLS.
- If the patient is required to undergo electrosurgery, minimize the energy that may affect the Evoke System:
    - Turn off stimulation.
    - Disconnect the eCLS if this is in use.
    - Ensure all fields, electrodes, probes and/or ground plates are as far away as possible from the Evoke System.
    - Use the lowest energy setting needed for the therapy.
    - Check the functioning of the Evoke System after the procedure and contact Saluda Medical if any problems are apparent.
    - Use bipolar mode if available.

⚠ Interference with implanted cardiac devices

- The Evoke System may interfere with other implanted stimulators with sensing capabilities, such as demand type pacemakers or cardioverter defibrillators.
- The effects of implanted stimulation devices on the Evoke System is unknown.

⚠ Stimulator damage

- If the CLS case is ruptured or pierced, then patient tissue may be exposed to battery chemicals, which could lead to burns or tissue damage.
    - Do not implant the CLS if the case is damaged.

⚠ Electromagnetic interference

- Strong electromagnetic fields may turn the stimulator off, cause uncomfortable or jolting stimulation or affect communication with the EPC.
- Patients should be advised to avoid or turn stimulation off around:
    - Security screeners, such as those used at department stores, public buildings, and airports – patients should present their implantable device ID card and request to go around the screener. If they are required to go through the screener they should turn stimulation off.
    - Power lines or power generators.
    - Electric steel furnaces and arc welders.
    - Large, magnetized stereo speakers.
    - Tag deactivators, such as those found in retail stores and libraries.
    - Radio communication transmitters or antennas, such as CB radio antennas (see Section 17.4).
- Patients should be advised to seek medical advice before entering any environment that may adversely affect the operation of their stimulator, including areas protected by a warning notice preventing entry by patients fitted with a pacemaker.

⚠ Heat due to charging

- During charging, the Charger, Charger coil, and/or CLS may become hot.
- Patients should not charge while sleeping, or with the Charger coil wrapped in blankets or clothing for prolonged periods, as this may result in heating leading to redness, skin irritation, or a burn.
- Patients should ensure there are no metal objects between the Charger coil and the stimulator during charging, as the metal object may heat up and cause redness, skin irritation, or a burn. Additionally, the Charger may not operate correctly.
- The Charger unit may become hot during use, with a surface temperature reaching 48 °C (118 °F). Patients should be advised not to hold the Charger unit for longer than 10 minutes during use to prevent risk of skin irritation, redness or injury.
- If patients experience pain or discomfort, they should cease charging and contact Saluda Medical.

⚠ Allergic reaction to system components

- If the patient may be allergic to system components they should not be implanted.
- Please refer to Section 17.2 for a list of materials in the system.
- Contact your Saluda Medical Representative for more information if necessary.

⚠**Use in diabetic patients:**

Surgical complications and adverse events may be more frequent and severe in diabetic patients. The following additional considerations should be made for diabetic patients including:

- A pre-operative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease, those with autonomic neuropathy or renal failure, and patients with a Hemoglobin A1C (HbA1c) ≥ 8% (64mmol/mol).
- Monitor the patient's blood glucose levels in the perioperative period and instruct the patient to continue to monitor levels as they may fluctuate as a response to surgery or to complications. Implanting physicians and/or anesthesiologists should consult practice guidelines for the interoperative management of diabetic patients during surgery.
- Closely monitor the patient for signs of infection, delayed wound healing, or cerebrospinal fluid (CSF) leakage as the severity of these complications may be greater in diabetic patients.
- The physiologic closed-loop controlled (PCLC) stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.
- Frequencies greater than 1200 Hz have not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

⚠**The Evoke System has not been tested for use in patients who are pregnant or nursing.**

⚠**The Evoke System has not been tested for use in patients under 18 years old.**

4.2 Precautions

⚠**Physician training**

- Implanting physicians should be trained in SCS procedures.
- Physicians should review this surgical manual before surgery.

⚠**Medical imaging**

- MEG, PET, x-ray/fluoroscopy and diagnostic ultrasound are unlikely to affect the Evoke System.

⚠ Medical therapies

When used in close proximity to the Evoke System, the following medical therapies may turn stimulation off or cause damage to the CLS:

- Ultrasonic scanning
- High-output ultrasound
- Lithotripsy

Implanted parts of a system should not be exposed to therapeutic levels of ultrasound energy as the implantable parts can inadvertently concentrate the ultrasound field and cause harm.

- Electrocautery or electrosurgical diathermy
- External defibrillation
- Radiation therapy (any damage to the device by radiation may not be immediately detectable)
- TENS
- Psychotherapeutic procedures (e.g. electroconvulsive therapy, transcranial magnetic stimulation)
- Laser procedures

If the patient is required to undergo any of these therapies, minimize the energy that may affect the Evoke System:

1. Turn off stimulation.
2. Disconnect the eCLS if this is in use.
3. Ensure all fields, electrodes, probes and/or ground plates are as far away as possible from the Evoke System.
4. Use the lowest energy setting needed for the therapy.
5. Check the functioning of the Evoke System after the procedure and contact Saluda Medical if any problems are apparent.
6. Use bipolar mode if available.

⚠ Operating equipment

The Evoke System is an SCS system that measures the patient's Evoked Compound Action Potentials (ECAP) in response to stimulation and adjusts the amplitude of stimulation in order to maintain stable coverage of painful areas. This is known as ECAP-controlled closed-loop stimulation.

- If the Evoke System has closed-loop stimulation enabled, patients may leave stimulation on while operating automobiles, other vehicles, or potentially dangerous equipment.

- During charging closed-loop is disabled, so patients should turn stimulation off if charging while driving or operating equipment.
- If the patient experiences sudden changes in stimulation with closed-loop enabled, they should turn stimulation off before driving or operating equipment. In this case, the patient should contact the clinic to reprogram the closed-loop settings of the stimulator.

When operating with closed-loop stimulation disabled, the Evoke System may produce sudden changes in stimulation that may distract patients while driving or operating equipment.

- If the Evoke System has closed-loop disabled, patients should turn stimulation off before operating automobiles, other vehicles, or potentially dangerous equipment.

⚠ Post-operative patient instructions

- After implantation of the Evoke System, patients should take care to allow adequate healing and ensure that the leads and CLS do not move.
- For six to eight weeks after surgery, patients should avoid:
    - lifting more than 11 lbs. (5 kg);
    - physical activities requiring stretching, bending or twisting;
    - raising their arms above their head repetitively.
- Patients may experience temporary pain at the implant site as the incisions heal after the surgery.
- Patients may experience redness or irritation at the implant site, in which case they should contact their physician to check the wound for infection or adverse reaction to the implanted materials.

⚠ Stimulator manipulation

- Patients should avoid manipulating the Evoke System through the skin. This may cause damage to the system, which could stop therapy, and may require surgery to rectify. Such manipulation of the device could also lead to painful tissue damage or skin erosion.
- If the CLS is “flipped” over inside the skin pocket it may no longer be able to be charged.

⚠ Scuba diving

- Patients should always obtain advice from their clinician prior to any diving activities.
- Patients should not dive below 16 ft. (5 m) or use hyperbaric chambers above 1.5 atm (150 kPa).
- The CLS may be damaged at greater depths or pressures.

⚠ Sterilization, storage and operation

- All surgical and implantable components of the Evoke System are supplied sterile.
- The sterile components of the Evoke System are sterilized using ethylene oxide.
- All sterilized components of the Evoke System are single use only, and should not be re-sterilized or reused, because of the risk of infection and device malfunction.
- Please observe and use infection control procedures of the accredited site where procedure is being performed.
- Please observe the storage conditions printed on the labels of each component – particularly storage and transport temperature and humidity, which varies between components – as inadequate storage could have a negative impact on operation, shelf-life and sterility.
- Please observe the expiration dates printed on the labels and return any expired product to Saluda Medical because of the risk of infection.
- Do not use surgical or implantable components if the package appears to be damaged or has been previously opened. If the packaging appears to be damaged, please return it to Saluda Medical for replacement.
- Visually inspect the stainless-steel components of the device for evidence of rust prior to use. If any rust (corrosion) is visible, the devices should be discarded.
- All sterile products are packaged in an outer sealed tray or pouch and should be opened with care to maintain sterility of the contents. The sterile contents of the tray or pouch should only be handled inside the sterile surgical field.
- The CLS is packaged in an inner and outer tray. Only the outer tray is the validated sterile barrier and therefore the inner tray should not be placed back into storage once it is taken out of the outer tray.
- Handle system components carefully to protect them from striking hard surfaces or being dropped.
- Do not use system components if they appear damaged, broken or malfunctioning as this may result in electrocution or excess heat generation causing burns or tissue damage.
- Stop using the eCLS if it becomes warm during use.
- Do not get the eCLS wet.
- Patients should be advised to avoid storing or using the Evoke external accessories outside the labeled temperature ranges or in hot or steamy environments, such as bathrooms, and to keep them dry.
- Patients should be advised to refer to the Evoke SCS System User Manual for guidelines for safe use of batteries in the Evoke System.

⚠ Modifications to System

- The components of the Evoke System are not intended to be modified by users or surgeons in any way.
- Do not modify or tamper with the Evoke Patient Controller (EPC), the Charger or the external Closed-Loop Stimulator (eCLS). Modifying or tampering with system components could cause malfunctions, unpredictable device behavior or failure, leading to harm to the patient.
- Do not connect anything to the eCLS or Charger that is not supplied as part of the Evoke System. The eCLS should only be connected to intraoperative cables or lead adapters by the clinician
- The Charger should only be connected to the supplied power adapter. Connecting these devices to other, unsupported items could damage them and lead to a loss of therapy.
- Only use the supplied eCLS battery and only charge the eCLS battery with the supplied eCLS battery charger. Refer to the Safety Precautions sheet provided with the eCLS battery charger.
- Use of accessories, transducers, and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

⚠ Lead Extension

- The Lead Extension should only be used as part of a trial system, to connect the lead to the eCLS (via the lead adapter). It should **not** be implanted for connection to an implanted CLS.
- Use of the Lead Extension for permanent implant carries a risk of disconnected electrodes, possibly leading to loss of stimulation therapy and requiring device revision.
- For permanent implant do not use a lead extension; select the permanent lead length (60 or 90 cm) appropriate for the patient and intended implant location.

⚠ Protection of external system components; eCLS, EPC and Charger

The electronics in external devices in the Evoke System such as the eCLS, Charger and, EPC, can be damaged by moisture, extreme heat, cold and humidity.

- Avoid storing the eCLS at temperatures below -10°C (14 °F) or above 55 °C (131 °F).
- Avoid storing the EPC and Charger at temperatures below -20 °C (-4 °F) or above 60 °C (140 °F).
- Only use the eCLS and EPC at room temperatures of 5 °C (41 °F) to 40 °C (104 °F).

- Only use the Charger at room temperatures of 5 °C (41 °F) to 30 °C (86 °F). Do not use the Charger if the room temperature is above 30 °C (86 °F).
- The eCLS is not moisture resistant whilst the case is open. Take care that the eCLS does not come into contact with liquids whilst the case is open. Wetting of the eCLS whilst out of its case may cause device malfunction or failure, leading to ineffective therapy for the patient.
- External system components should be kept dry and never be immersed in water.
- Handle external system components carefully to protect them from striking hard surfaces or being dropped.
- The Charger should not be plugged into outlets that are in humid environments or near water.
- The Serial connection  on the Charger is for Saluda Medical representative use only. This connection is protected by a silicone plug. Ensure the plug is fully inserted at all times.
- Instruct patients not to leave devices in their car or outdoors for extended periods of time.
- Instruct patients not to store devices in humid environments, such as the bathroom.
- Instruct patients to allow devices to reach room temperature for 30 minutes before use if they have been stored in cold or warm conditions.
- Instruct patients to ensure they can always access their EPC and to keep a spare set of AAA batteries at home for the EPC.
- Instruct patients to plug in the power adapter for the Charger somewhere easy to access.
- If any external system components require cleaning, refer to Section 15 ‘Maintenance of the Evoke eCLS, EPC, and Charger’.

⚠ Battery care

The EPC is powered by two disposable AAA alkaline batteries. Observe the following guidelines for safe use of batteries with your EPC:

- Insert batteries in the correct orientation by observing the plus (+) and minus (-) marks on the batteries and the EPC.
- Do not mix batteries that differ by manufacturer, brand, type, age or previous usage.
- Replace both batteries at the same time.
- Do not touch the battery contacts in the EPC.
- Do not short-circuit batteries (e.g. do not let terminals of batteries contact each other, do not store batteries loosely).

- Do not disassemble, deform, immerse in water, or dispose of batteries in fire.
- Wipe batteries with a clean dry cloth if they become dirty.
- Store unused batteries in original packaging, in a clean and dry place.
- Do not use damaged or deformed batteries. If skin or eyes come into contact with battery fluid or liquid, wash out with water and seek medical attention immediately.
- Do not expose batteries to heat.
- Do not recharge batteries.
- Dispose of used batteries promptly and carefully, in accordance with local regulations. Keep away from children.

The Charger is powered by internal rechargeable lithium ion batteries that cannot be replaced:

- Only the power adapter supplied by Saluda Medical should be used to recharge the Charger.
- The power adapter socket on the Charger should not be touched.
- The Charger power adapter should be unplugged from the charger after recharging is complete.

The eCLS is powered by a rechargeable, replaceable lithium ion battery:

- Only the supplied battery should be used to power the eCLS.
- Only the supplied eCLS battery charger should be used to recharge the eCLS battery.
- Do not cover the eCLS battery or charger whilst recharging the battery.
- Avoid the eCLS battery being dropped or striking hard surfaces. Damage to the eCLS battery could cause leakage, overheating or explosion.
- Do not use the eCLS battery if it is damaged or deformed. If skin or eyes come into contact with battery fluid or liquid, wash out with water and seek medical attention immediately.
- Do not disassemble, deform, immerse in water, or dispose of eCLS battery in fire.

⚠ Device malfunction or failure

Therapy should be discontinued immediately in the event of malfunction or failure of any component of the Evoke system.

- Malfunction or failure may be indicated by excessive device heating, emission of smoke or strange smell, or abnormal device behavior.
- Continued use of system components after malfunction or failure may cause electrocution, burns, tissue damage or uncomfortable stimulation for the patient.
- Please contact Saluda Medical in the event of any device malfunction or failure.

⚠ Disposal of Evoke System Components

- Do not dispose of the CLS, eCLS, EPC or Charger devices. These devices contain batteries that could explode if they are thrown into a fire.
- All explanted, malfunctioning or failed Evoke devices should be returned to Saluda Medical.

4.3 Potential risks

Every surgery involves potential risks, including death. In addition to these surgical risks, the risks associated with the implantation and use of a spinal cord stimulation system include:

- Undesirable changes in stimulation sensation and/or location.
- Uncomfortable changes in stimulation (over and/or under stimulation).
- Temporary or persistent post-surgical pain at hardware implantation sites.
- CLS migration or suboptimal placement, which may result in pain or difficulty in charging.
- Seroma or hematoma at surgery sites.
- Epidural haemorrhage, spinal cord injury, possible paralysis or other neurological complications.
- Lead migration or suboptimal placement, which may result in undesirable stimulation changes.
- Breakage of the lead, or malfunction or failure of other system components, which may result in undesirable changes or loss of stimulation.
- Allergic response or tissue reaction to the implanted or external materials.
- Infection that may require hospitalisation with intravenous antibiotic therapy.
- Infection may result in epidural abscess that can lead to neurological harm.
- Cerebrospinal fluid (CSF) leakage with possible fistula formation.
- Gastrointestinal and/or genitourinary disruption or compromise.
- Inadequate pain relief following system implantation or over time.
- Erosion of the implanted components through the skin.
- Weakness, clumsiness, numbness, abnormal sensations or pain.
- Skin irritation.

The patient may require surgery (including revision, explant, and replacement) as a result of any of the above.

Note: Diabetic patients may have increased risks of infection, problems healing around the surgical site, and complications common to any surgical procedure. The severity of any surgical complication may be greater in diabetic patients, particularly those with inadequate pre-operative glycemic control.

5 Percutaneous lead implant procedure

5.1 Overview

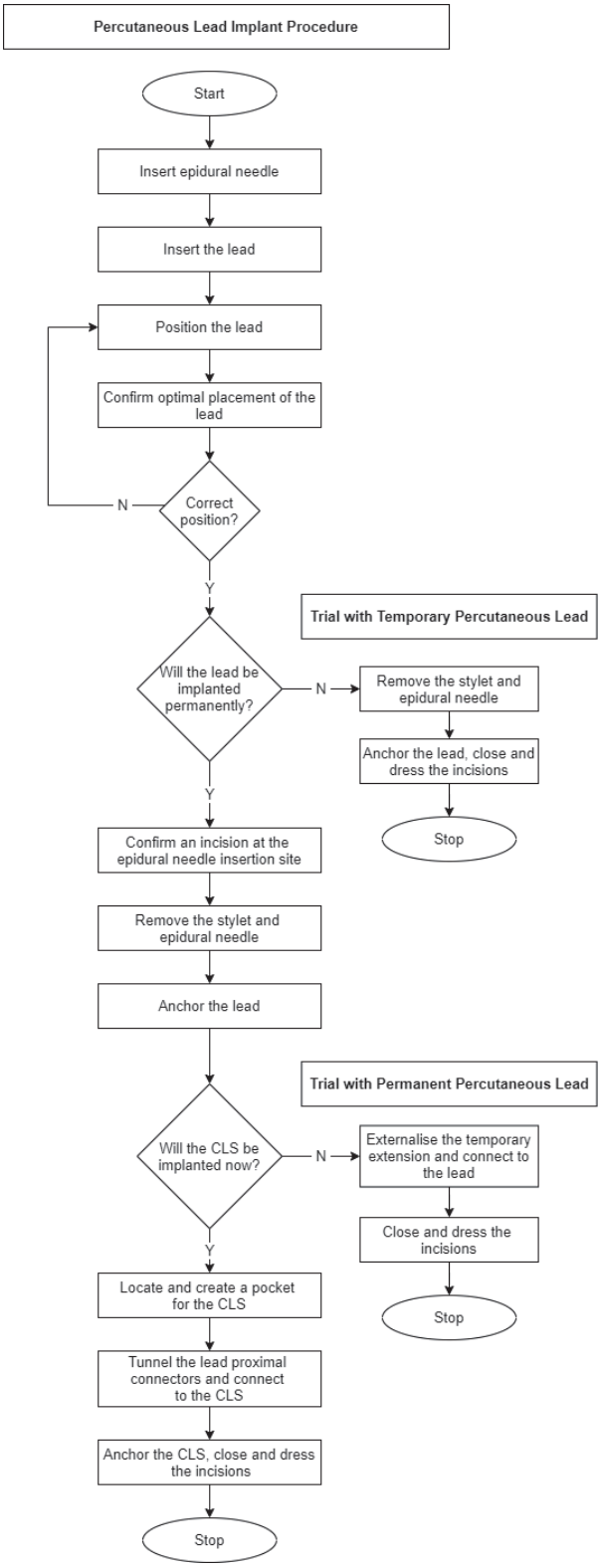


Figure 5.1: Overview of the percutaneous lead implantation process.

5.2 Percutaneous lead placement

5.2.1 Insert the epidural needle

1. Mark the patient's back using fluoroscopy for the required vertebral level.

   ⚠ **Warning:** The risk of patient injury increases as the needle insertion site moves up the spinal column from lumbar to cervical.

   Select an insertion site that provides the widest and easiest possible access to the epidural space to reduce the risk of patient injury due to spinal cord trauma.

   ⚠ **Caution:** It is recommended that the patient remain communicative during needle and lead placement to help mitigate any risk of neural injury.

2. Using an Epidural Needle from the surgical tools, insert the needle with the bevel up and a paramedian approach (refer to Figure 5.2) no greater than 45° angle to the skin into the epidural space (refer to Figure 5.3).

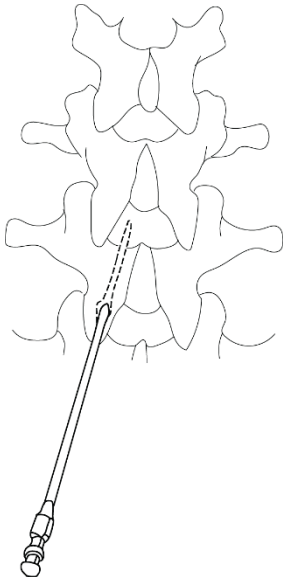


Figure 5.2: Inserting the needle with a paramedian approach.

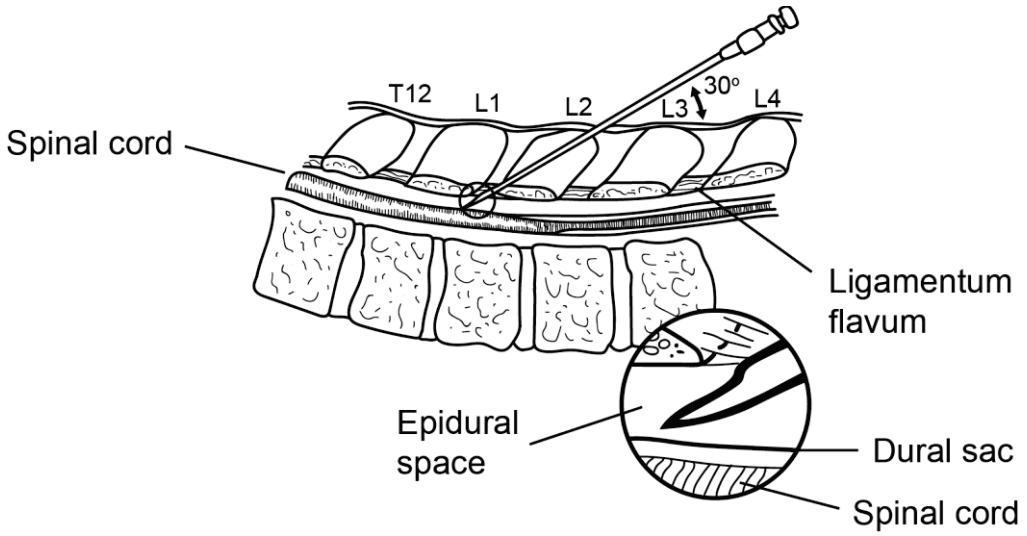


Figure 5.3: Insert the needle at no greater than 45°.

3. Confirm that you have entered the epidural space using a loss of resistance check.

5.2.2 Insert the percutaneous lead

1. Feed the percutaneous lead with the stylet, through the needle into the epidural space (refer to Figure 5.4).

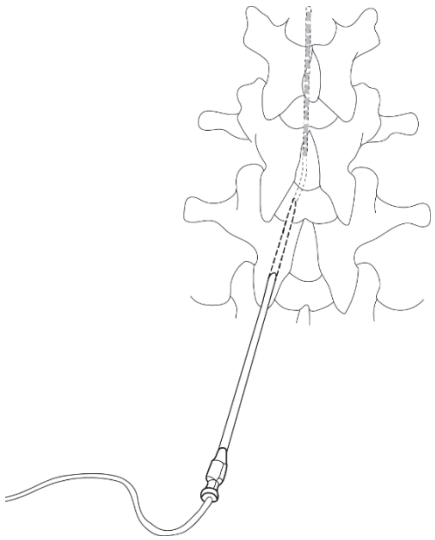


Figure 5.4: Feeding the percutaneous lead and stylet through the needle.

5.2.3 Position the percutaneous lead

1. Use the stylet handle to rotate and guide the percutaneous lead with one hand as you advance it with the other, while viewing it under fluoroscopy.
2. Continue advancing the percutaneous lead to the required location.
   - The percutaneous lead is pre-loaded with the bent stylet.

- You can replace the bent stylet with the straight stylet if required.

5.2.4 Confirm optimal placement of the lead

Physicians may have a preference on the method to confirm optimal lead placement in the operating room. Lead position may be confirmed anatomically using fluoroscopy, incorporating ECAP measurement, and/or through paresthesia mapping using intraoperative patient feedback.

Following lead placement based on required anatomical location, the surgeon connects the leads to the intraoperative cables inside the sterile field. The surgeon passes the end of the cables out of the sterile field to the programming clinician.

For intra-operative testing methods, refer to Section 10 'Intra-operative testing'. For intra-operative programming guidance, refer to the Evoke SCS System Clinical Manual accessible at https://www.saludamedical.com/manuals.

5.2.5 Create an incision at the epidural needle insertion site

Note: If the percutaneous lead will be externalized for a trial period, go to Section 7 'Trial with a temporary percutaneous lead', otherwise continue.

1. Create an incision around the needle sufficiently large to accommodate a strain relief loop if required (refer to Section 5.4) and the anchors for each percutaneous lead.

5.2.6 Remove the stylet and epidural needle

1. Carefully withdraw the epidural needle from the insertion site by sliding it along the percutaneous lead until clear of the body.
2. Carefully withdraw the stylet from the lead ensuring that the percutaneous lead position does not change.
3. Slide the epidural needle completely from the percutaneous lead.
4. Confirm lead position with fluoroscopy if required (and adjust position if needed).
5. Proceed to Section 5.3 'Anchor the lead'.

5.3 Anchor the lead

⚠ **Caution:** Suturing directly to the lead may damage the lead or cause it to fail.

The Evoke CAP12 Percutaneous leads are compatible with the following anchors:

1. Saluda Medical Evoke Suture Anchor.
2. Saluda Medical Evoke Active Anchor.
3. Medtronic Bi-Wing Injex Anchor (Model 97792)
4. Medtronic Bumpy Injex Anchor (Model 97791)

5.3.1 Position the anchor

1. Prepare the anchors for insertion by wetting with saline.
2. Slide the anchor (refer to Figure 5.5A) or suture anchor (refer to Figure 5.5B) over the proximal connector end of the lead.
3. You may encounter some initial resistance as the proximal end has a stiffened section with a larger diameter. After feeding the lead into the anchor, grip the proximal connector end of the lead with your fingers and slide the anchor onto the lead.

   ⚠ **Caution:** Do not use surgical instruments to grip the proximal connectors

4. Slide the anchor along the lead until the distal portion of the anchor is at the lead entry site (refer to Figure 5.5).



Figure 5.5: A) An active anchor positioned on a percutaneous lead.

B) A suture anchor positioned on a percutaneous lead.

5.3.2 Secure the anchor

1. Secure the anchor to the supraspinous ligament or deep fascia with 2 or 3 non-absorbable sutures looped through the suture holes on the anchor and/or in the grooves around the circumference of the anchor.

   ⚠ **Caution:** Do not use polypropylene sutures on the silicone anchor, as the polypropylene may damage or cause the anchor to fail.

5.3.2.1 Evoke Active anchor

1. Fit the head of the torque wrench (Figure 5.6A) supplied in the kit into the setscrew in the active anchor (refer to Figure 5.6B).

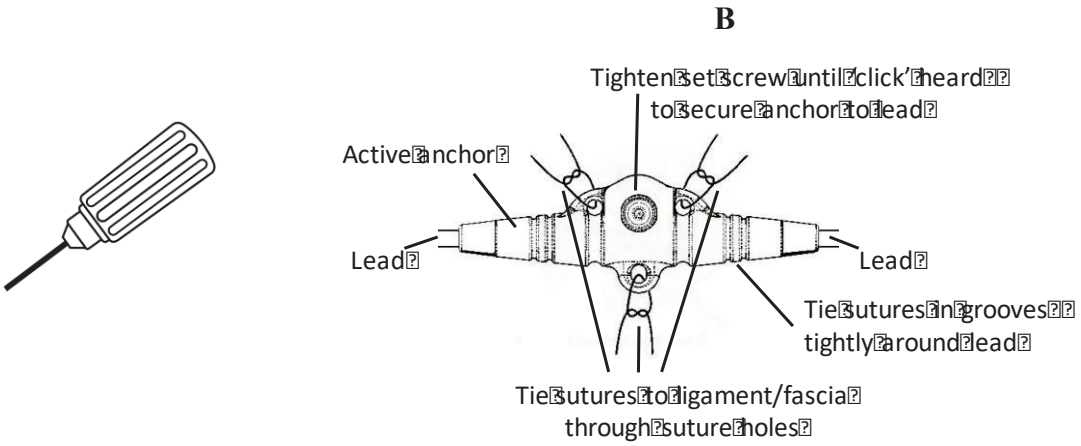


Figure 5.6: A) Torque wrench. B) Active anchor with screw secured against lead.

2. Use the torque wrench to gently tighten the setscrew clockwise until you hear a "click".
3. If needed, tie 1, 2, or 3 sutures in the grooves around the circumference of the anchor to secure the anchor to the lead (refer to Figure 5.6).

5.3.2.2 Evoke Suture anchor

1. Tie two sutures in the grooves around the circumference of the anchor.
2. Ensure the suture is tied tightly to minimize lead movement in the anchor (refer to Figure 5.7).

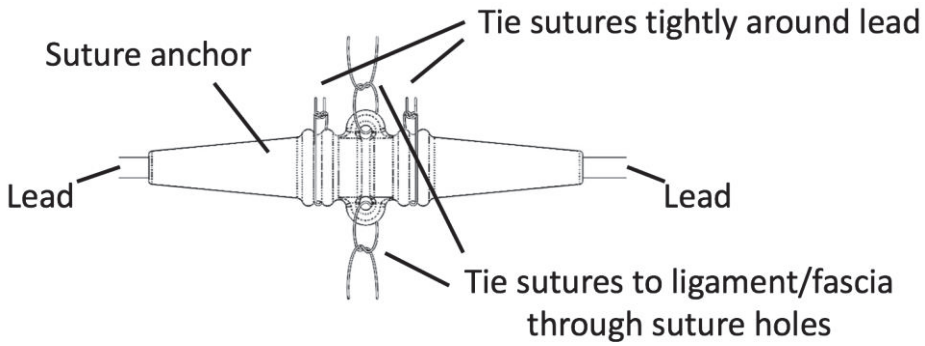


Figure 5.7: Securing the suture anchor.

5.3.2.3 Medtronic Injex Anchor

Refer to Medtronic's Instructions for Use, which are provided in the Injex product box.

5.4 Create a strain relief loop in the lead

1. A strain relief loop in the lead may be used to provide some slack and minimize tension on the lead due to body movement. If you consider the anchoring technique sufficient to minimize lead migration, the loop may not be required.

2. Using blunt dissection, create a small subcutaneous pocket at the incision site for a small loop of lead and lead extension connector blocks if used.
3. Create a loop in the lead and insert into the small pocket (refer to Figure 5.8).

   ⚠ **Caution:** In some patients, the loop may move or flip producing a lump under the skin and cause discomfort or problems at the anchor site wound, such as granuloma or infection.

   - If the CLS is to be implanted, proceed to Section 6 ‘Lead tunneling and CLS implant procedure’.
   - If a temporary extension will be externalized for a trial period proceed to Section 8 ‘Trial with a percutaneous extension’.

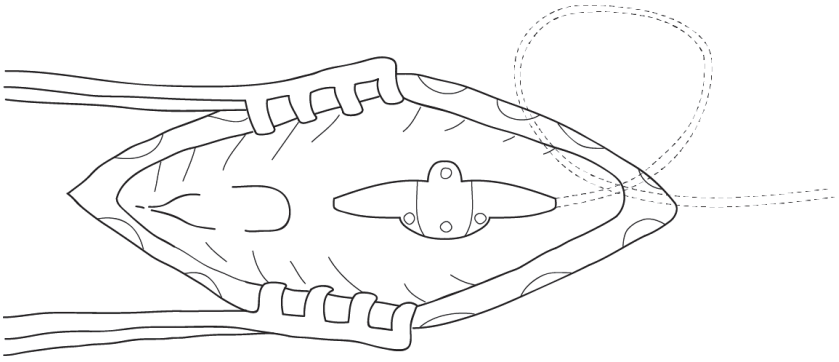
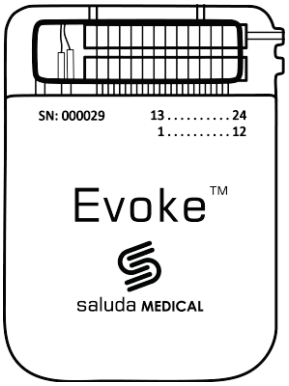


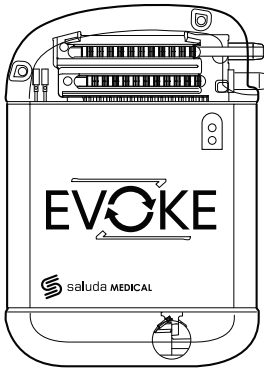
Figure 5.8: Small subcutaneous pocket for the strain relief loop and lead extension if used. Note that the strain relief loop should be on the CLS or lead extension side of the anchor.

6 Lead tunneling and CLS implant procedure

Two CLS versions are available, REF 3002 and REF 3042 (Figure 6.1). The two versions are similar or equivalent in size and functionality and the following instructions, which show REF 3042, apply to both versions.



REF 3002



REF 3042

Figure 6.1: REF 3002 and REF 3042 versions of the CLS.

6.1 Locate and create a pocket for the CLS

Typically, the pocket is located in soft subcutaneous tissue at the top of the buttocks or on the patient's flank.

1. Mark the location for the incision and mark the size of the pocket required.
    - The pocket should be the same size as the CLS.
2. Create an incision with a scalpel and a subcutaneous pocket with blunt dissection.
    - The pocket should 0.5 cm to 2 cm (0.2 in to 0.8 in) below the skin surface.

⚠ **Caution:** Ensure that the CLS is not implanted too superficially, so that the risk of pain and skin erosion is minimized, or too deep so that charging is not compromised.

6.2 Tunnel the lead

1. Create a pocket for the coiled leads (refer to Section 5.4).
    - For a single pass tunneling procedure (when the required tunnel is shorter than the tunneler) proceed to Section 6.2.1.
    - For an intermediate incision point tunneling procedure (when the required tunnel is longer than the tunneler) proceed to Section 6.2.2.

6.2.1 Using a single tunneling pass

Note: Two leads can be tunneled at the same time.

1. Create a pocket at the lead insertion site for the lead strain relief loop if required (refer to Section 5.4).
2. Insert the tunneler subcutaneously from the lead incision site to the CLS pocket.
3. Withdraw the tunneler, leaving the straw in the tunnel.
4. Slide the percutaneous lead proximal connectors through the straw of the tunneler to the CLS pocket.
5. Gently slide the straw out of the tunnel, towards the CLS pocket, and off the end of the percutaneous lead.
    - To connect the lead to the CLS proceed to Section 6.3.

⚠ **Caution:** Ensure that the leads are tunneled subcutaneously and are not too superficial, so that the risk of pain and skin erosion is minimized.

6.2.2 Using an intermediate incision point

Note: Two leads can be tunneled at the same time.

1. Create a pocket at the lead insertion site for the lead strain relief loop if required (refer to Section 5.4).
2. Create an intermediate incision between the lead incision site and the CLS pocket.
3. Insert the tunneler subcutaneously from the lead incision site to the intermediate incision site.
4. Withdraw the tunneler, leaving the straw in the tunnel.
5. Slide the lead through the straw of the tunneler to the intermediate incision point.
6. Gently slide the straw out of the tunnel, towards the intermediate incision point, and off the end of the percutaneous lead.
7. Re-attach the tunneler straw to the tunneler and tunnel subcutaneously from the intermediate incision site to the CLS pocket.
8. Withdraw the tunneler, leaving the straw in the tunnel.
9. Slide the lead through the straw of the tunneler to the CLS pocket.
10. Gently slide the straw out of the tunnel, towards the CLS pocket, and off the end of the lead.
    - To connect the lead to the CLS proceed to Section 6.3.

⚠ **Caution:** Ensure that the leads are tunneled subcutaneously and are not too superficial, so that the risk of pain and skin erosion is minimized.

6.3 Connect to the CLS

1. Wipe down the lead proximal connectors prior to insertion into the CLS to ensure that contacts are clean and dry.
2. Slide the proximal connector end of the lead into its port in the header of the CLS (refer to **Figure 6.2**).
    a. Lead 1, electrodes 1-12, insert into the lower port.
    b. Lead 2, electrodes 13-24, insert into the upper port.

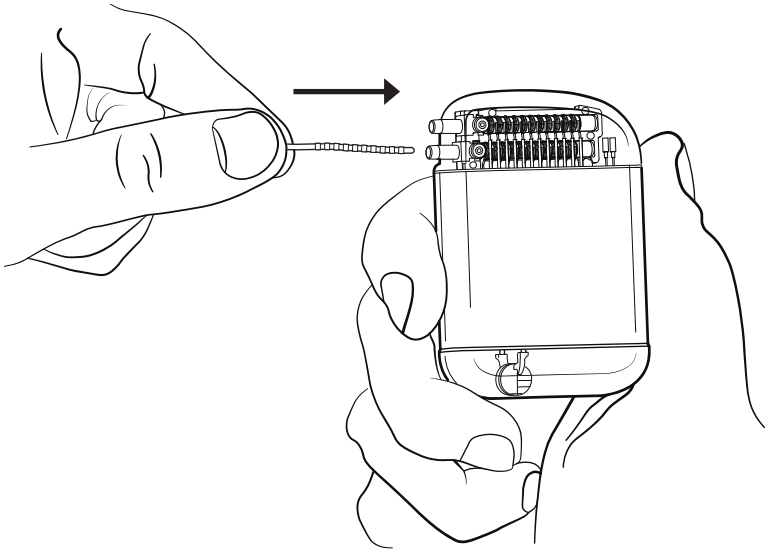


Figure 6.2: Inserting the proximal connectors into the CLS header.

3. Gently slide the proximal connector until it hits a stop.
    a. All contacts should be within the port.
    b. The end of the proximal connector should rest against the stop – visible through the header.

    Note: Take care to ensure that there is no bend or kink in the lead while inserting.

4. Temporarily place the CLS partially within the CLS pocket.
5. Confirm correct connection.

    Note: This step is to be completed by the programming clinician outside of the sterile field. The Evoke SCS System Clinical Manual provides specific information on this procedure. The programming clinician:

    a. Initiates wireless communication between the CI and the CLS.
    b. Checks the impedance with the CI to ensure that any leads are connected properly to the CLS.
    c. It may be necessary to reinsert the leads if some electrodes are not connected properly to the CLS.

When satisfied that the leads are correctly inserted, use the torque wrench (supplied in the CLS kit) to tighten the setscrew on each port until you hear a “click” (refer to Figure 6.3).

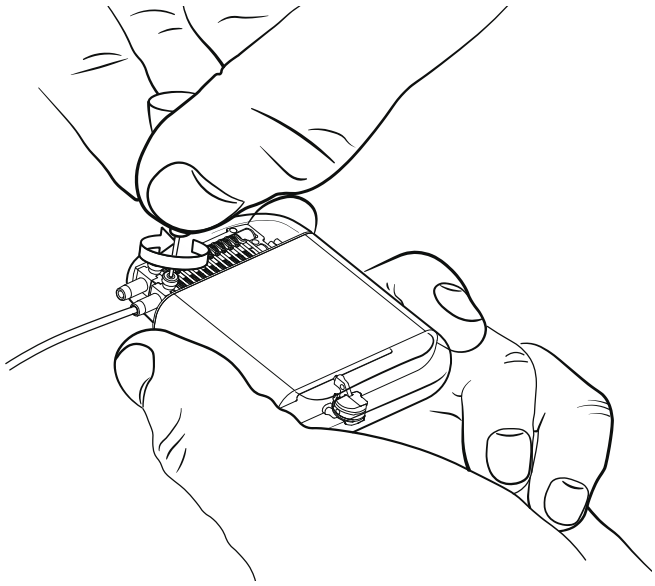


Figure 6.3: Tightening the port screws until you hear a "click".

6. If you are using only one lead, place the CLS port plug in the unused port to prevent moisture ingress (refer to Figure 6.4:). Ensure that you push the port plug into the silicone strain relief.

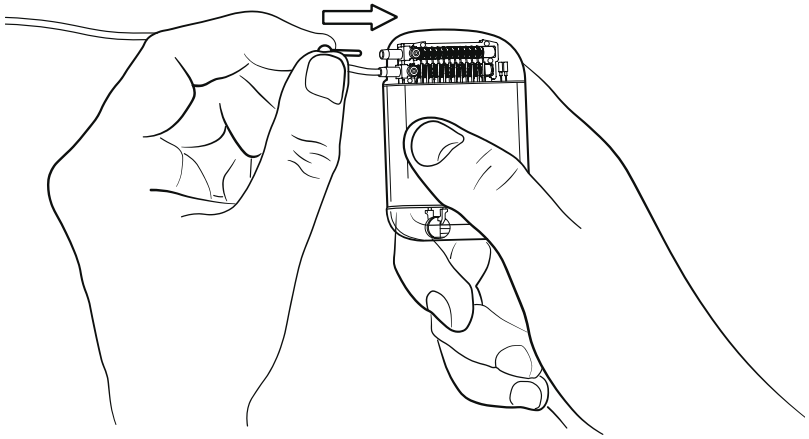


Figure 6.4: Inserting the port plug.

7. Tighten the setscrew with the torque wrench (supplied in the kit) until you hear a “click”.
8. Check that the port plug is secured and will not pop out after tightening the set screw.
9. Create a strain relief loop under the CLS (refer to Figure 6.5). If there is excess lead after this loop, coil the lead around the perimeter of the CLS or underneath.

Note: The strain relief loop takes up any excess length and reduces tension in the lead during movement.

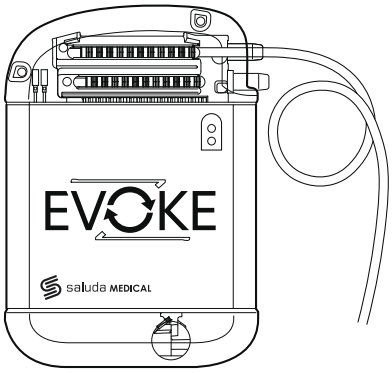


Figure 6.5: The lead exiting the CLS header with a strain relief loop.

⚠ **Caution:** Ensure that the lead is not bent at the port entry of the CLS header (refer to Figure 6.6).

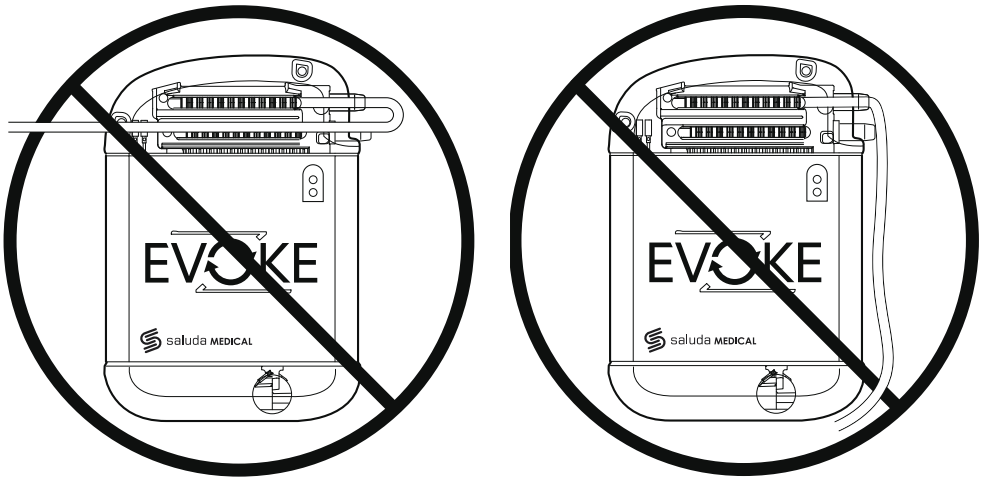


Figure 6.6: Examples where the lead has been bent at the port of entry of the CLS header. Take care to avoid this when creating the strain relief loop.

6.4 Anchor the CLS, close and dress the incisions

1. Insert the CLS into the pocket with the looped lead under the CLS.
2. Ensure that the writing on the CLS is facing up towards the skin so that charging will be possible.
3. Ensure that the CLS is between 0.5 cm to 2.0 cm (0.2 in and 0.8 in) under the skin so that charging will be possible.
4. Ensure that the CLS lays parallel to the skin surface so that charging is not compromised.
5. Secure the CLS to the subcutaneous fascia with sutures through the holes in the header of the CLS.
6. Close and dress the incisions taking care that the leads are not damaged in the closing

process.

6.5 Post-operative procedures

For post-operative procedures and programming refer to the Evoke SCS System Clinical Manual.

7 Trial with a temporary percutaneous lead

Note: After completing steps 5.2.1 to 5.2.4 proceed to Section 7.1.

7.1 Remove the stylet and epidural needle

1. Carefully withdraw the epidural needle from the insertion site by sliding it along the percutaneous lead until clear of the body.
2. Carefully withdraw the stylet from the lead, ensuring that the percutaneous lead position does not change.
3. Slide the epidural needle completely from the percutaneous lead.
4. Confirm lead position with fluoroscopy if required.

7.2 Anchor the lead, close and dress the incisions

1. Using preferred techniques, close and dress the incision at the lead insertion site.
2. Using preferred method, ensure that the lead is firmly attached to the skin to minimize potential lead migration during the trial period.

   ⚠ **Caution:** Do not suture directly to the percutaneous lead as it may damage the lead or cause it to fail.

7.3 Post-operative procedures

For post-operative procedures and programming refer to the Evoke SCS System Clinical Manual.

7.4 Removing a percutaneous lead at the end of a trial

1. Disconnect the lead adapter from the eCLS.
2. Disconnect the lead adapter from the proximal connector of the lead.
3. If the lead has been secured to the skin this will need to be released.
4. Grasp the percutaneous lead between your thumb and forefinger, as close as possible to the patient's skin.
5. Gently withdraw the percutaneous lead from the epidural space.

6. If the patient is not proceeding straight to implantation surgery then clean the exit site, close and dress the incision.

8 Trial with a percutaneous extension

8.1 Externalize the temporary extension and connect to the lead

8.1.1 Create a subcutaneous pocket for the coiled lead and lead extension connector block

1. Create a subcutaneous pocket for the connector block of the lead extension.
2. Tunnel the lead to the pocket creating a strain relief loop at the lead insertion site if required (refer to Section 5.4).

8.1.2 Tunnel the lead extension

1. Select an exit point for the lead extension, ensuring it avoids the intended CLS pocket site.
2. Make an incision at the exit point.
3. Assemble the tunneler and passing straw.
4. Tunnel subcutaneously from the lead extension exit point to the pocket.
5. Withdraw the tunneler, leaving the straw in the tunnel.
6. Insert the proximal connector end of the lead extension into the passing straw at the pocket site.
7. Push the body of the lead extension through the passing straw until the proximal connectors have exited the passing straw.
8. Remove the passing straw towards the lead extension exit site.

⚠ **Caution:** Ensure that the leads or lead extensions are tunneled subcutaneously and are not too superficial, so that the risk of pain and skin erosion is minimized.

8.1.3 Connect the lead extension to the lead

1. Wipe down the lead proximal connectors prior to insertion into the lead extension to ensure that contacts are clean and dry.
2. Insert the lead proximal connectors into the lead extension connector block (refer to Figure 8.1).

   Note: Take care to ensure that there is no bend or kink in the lead while inserting. Test impedance of the electrodes to confirm a good connection.

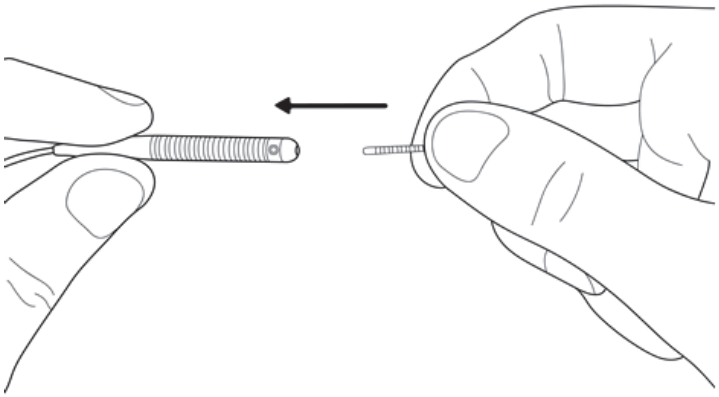


Figure 8.1: Inserting the lead proximal connectors into the lead extension connector block.

3. Gently slide the proximal connector until it hits a stop. All contacts should be within the connector block.
4. Confirm correct connection.
    - Connect lead extension to intraoperative cable to allow impedance measurement by an eCLS (refer to Section 10).

    Note: Impedance measurement is to be completed by the programming clinician outside of the sterile field. The Evoke SCS System Clinical Manual provides specific information on this procedure. The programming clinician:

    a. Initiates wireless communication between the CI and the eCLS.

    b. Checks the impedance with the CI to ensure that any leads are connected properly to the lead extension and eCLS.

    c. It may be necessary to reinsert the leads if some electrodes are not connected properly to the lead extension and eCLS.
5. Fit the head of the torque wrench (supplied in the kit) into the setscrew in the lead extension connector block (refer to Figure 8.2).
6. Gently tighten the setscrew clockwise until you hear a “click”.

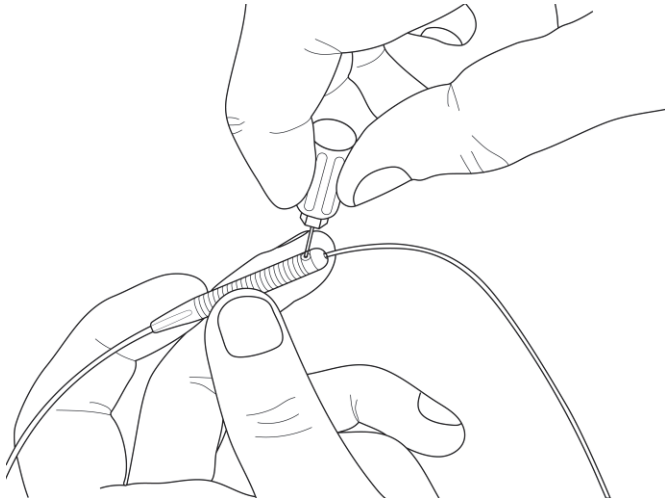


Figure 8.2: Tightening the set screw in the lead extension header block.

8.1.4 Place the lead, lead extension and connector block in the subcutaneous pocket

1. Coil the lead and subcutaneous section of the lead extension together with the connector block and carefully place in the pocket.
2. Place the connector block so it is easily accessible for later removal.

8.2 Close and dress the incisions

Using preferred techniques, close and dress the incision at the lead insertion site and the lead extension exit site.

⚠ **Caution:** Do not suture directly to the lead extension as it may damage the extension or cause it to fail.

8.3 Post-operative procedures

For post-operative procedures and programming refer to the Evoke SCS System Clinical Manual.

8.4 Removing a percutaneous extension at the end of a trial

1. Disconnect the lead adapter from the eCLS.
2. Disconnect the lead adapter from the proximal connector of the lead extension.
3. Remove external anchors or tape and clean the area around the lead extension exit site.
4. Gently pull the proximal end of the lead extension until 1-2cm is exposed from under the skin.
5. Using sterile scissors cut the newly exposed section of the lead extension and allow the implanted part to retract under the skin.

6. If the implant procedure is to be scheduled for a later date, then close and dress the exit site. Otherwise, continue with the following steps or complete these steps at the implant procedure.
7. Prepare the lead implant site for surgery using preferred procedure.
8. Re-open the incision created when implanting the lead and carefully expose the coiled lead and lead extension.
9. Using the supplied torque wrench, loosen the setscrew in the lead extension connector block and withdraw the lead from the extension connector block.
10. Remove and discard the implanted section of the lead extension.
11. If proceeding to CLS implantation, refer to Section 6 ‘Lead tunneling and CLS implant procedure’.
12. If not proceeding to implant then remove and discard the anchors and leads (see Section 9 ‘Revision, replacement and explant surgery’).

9 Revision, replacement and explant surgery

Surgery may be required in case of component failure, component movement, or site pain.

Note: Any component removed that is thought to be compromised should be returned to Saluda Medical for analysis via your Saluda Medical representative. All explanted CLS devices should be returned to Saluda Medical for proper disposal.

9.1 Open the component sites

1. Turn stimulation off using the patient’s EPC or the Clinical Interface (CI).
2. Surgically open the lead and/or CLS pocket sites as required.

   ⚠ **Warning:** Do not use electrosurgical techniques, such as electrocautery, over the leads or CLS, as this may cause tissue damage at the lead site and result in severe injury or cause damage to the CLS.

   ⚠ **Caution:** Take care with surgical instruments to ensure the leads and CLS are not damaged.
3. Cut any sutures and loosen setscrews with the torque wrench (supplied in the Spares kit) as required, to allow components to be moved.
4. Disconnect leads and CLS as required.

9.2 Percutaneous leads

1. If repositioning the lead:

a. Insert a stylet (supplied in the Spares kit) into the lead.

b. Guide the lead to the required position (refer to Section 5.2.3 to 5.2.4).

Note: For intra-operative testing methods, refer to Section 10 'Intra-operative testing'.

c. Anchor the lead (refer to Section 5.3 'Anchor the lead').

d. Tunnel the lead then connect to the CLS (refer to Sections 6.2 to 6.4).

2. If replacing the lead:

a. Insert the epidural needle or a flexible cannula over the existing lead into the epidural space and withdraw the existing lead.

Note: If it is difficult to insert the needle or cannula into the epidural space over the lead, a stylet may be inserted into the lead to stiffen it. Alternatively, the lead may be withdrawn, and the epidural needle inserted into a new location.

b. Insert the new lead (refer to Sections 5.2.2 to 5.2.4).

Note: For intra-operative testing methods, refer to Section 10 'Intra-operative testing'.

c. Anchor the lead (refer to Section 5.3 'Anchor the lead').

d. Tunnel the lead, then connect to the CLS (refer to Sections 6.2 to 6.4).

3. If explanting and not replacing, the lead/s and anchors may be removed and returned to Saluda Medical for investigation or disposal. Close and dress the incisions.

9.3 CLS

1. For CLS replacement, remove the existing CLS and connect the new CLS to the percutaneous lead (refer to Sections 6.3 to 6.4).

⚠ **Caution:** The leads may be difficult to insert if replacing an existing CLS: Ref No. 3042 with a new CLS: Ref No. 3002. Use new leads or a new CLS: Ref No. 3042 instead.

2. To move the existing CLS to a new site, create a new pocket, tunnel the percutaneous leads to the new pocket, connect and anchor the CLS, then clean and dress the incisions (refer to Section 6).

3. If explanting and not replacing, the CLS may be removed and returned to Saluda Medical for investigation or disposal. Close and dress the incisions.

10 Intra-operative testing

The following should be completed after lead placement based on required anatomical location (see Section 5.2.4)

10.1 Using the eCLS

The eCLS connects to 2x leads via 2x intraoperative cables.

The intraoperative cable consists of a lead adapter attached to the cable to connect to the lead at the distal end and a plug to insert into the eCLS at the proximal end (see Figure 10.1).

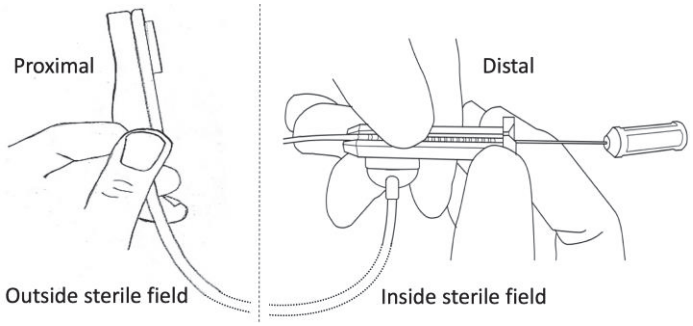


Figure 10.1: The intraoperative cable showing the proximal end after passing out of the sterile field and the distal end in the sterile field after inserting the lead proximal connector.

1. After connecting the lead to the distal end of the intraoperative cable (see Section 10.2), pass the proximal plug end of the cable out of the sterile field.
2. To connect a second lead and intraoperative cable repeat the above step.

   ⚠**Caution:** The eCLS is not moisture resistant whilst the case is open. Take care that the eCLS does not come into contact with liquids whilst the case is open.

10.2 Connect the lead to the intraoperative cable

⚠**Caution:** Avoid tension or pulling on the intraoperative cable whilst connected to avoid movement of the implanted leads.

1. Place the tip of the proximal connector end of the lead into the slot on the distal end of the intraoperative cable (see Figure 10.2). The stylet fits into the groove on the distal end.

   Note: It is not necessary to remove the lead Stylet.

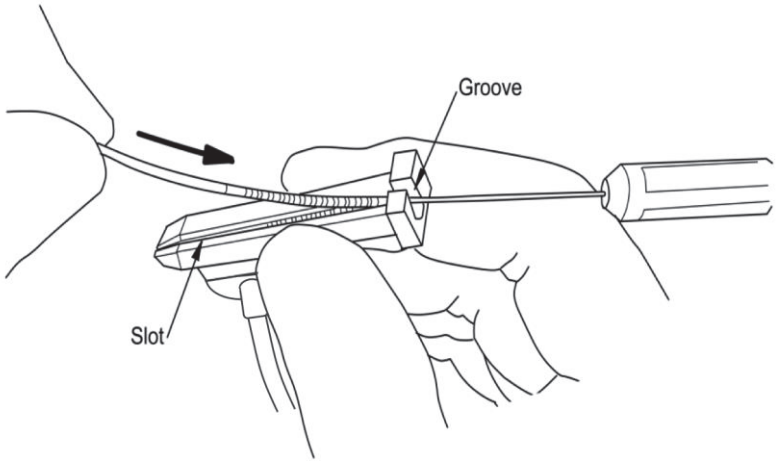


Figure 10.2: Placing tip of proximal connector into slot on the distal end of the intraoperative cable, with stylet fitting in groove.

2. Push the lead down into the slot completely using a finger (see Figure 10.3), so that the lead is flush with the top of the slot. The lead should not move when fully pushed into the slot. After the lead is in the slot, press down again along its length to ensure it is secure in the slot.

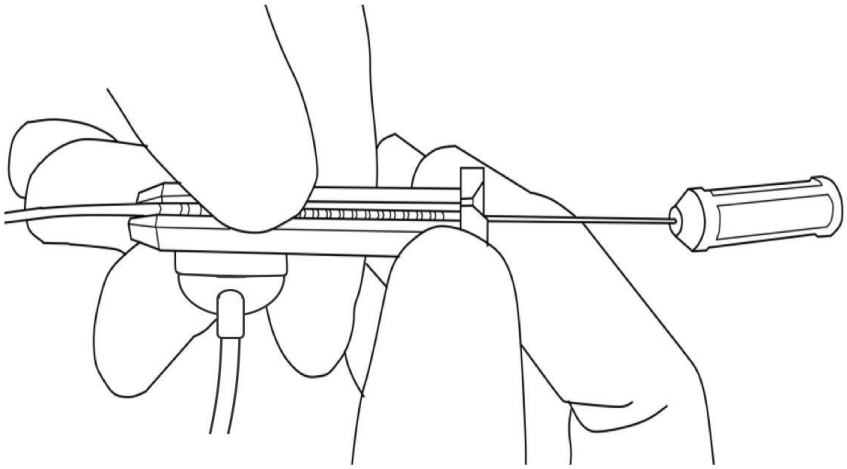


Figure 10.3: Pushing lead into slot.

3. Place the top cover of the distal end of the intraoperative cable over the lead, with the open side of the top cover aligned with the cable connection. Slide the top cover all the way onto the distal end until the notch on the top cover clips into place (see Figure 10.3).
4. To connect a second lead repeat the above steps.

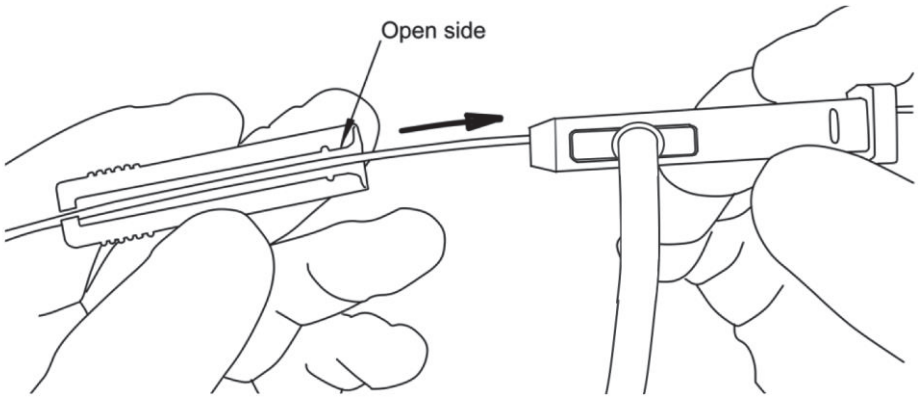


Figure 10.4: Placing the top cover over the lead and sliding onto distal end of the intraoperative cable until it clips into place.

10.3 Connect the intraoperative cable to the eCLS

This section is to be completed by the programming clinician outside of the sterile field.

⚠ **Caution:** Maintain a clear path between the patient and the eCLS whilst the intraoperative cable is connected to avoid tension or pulling on the implanted leads.

1. The programming clinician will plug the proximal end of the intraoperative cable into the port on the eCLS (refer to Figure 10.5).
2. To connect a second intraoperative cable, repeat the above step.

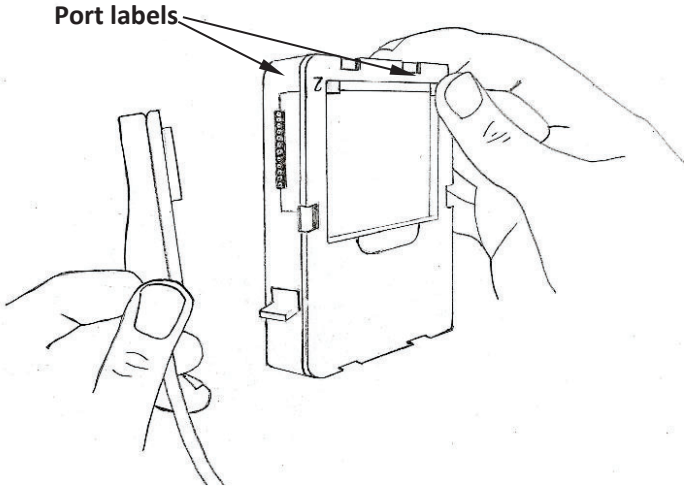


Figure 10.5: Connect the intraoperative cable to the eCLS. Port 2 (electrodes 13–24) is shown here. Port 1 (electrodes 1-12) is on the opposite side of the eCLS.

10.4 Confirm optimal lead placement

Confirmation of optimal lead placement may use one or more of the following methods to confirm medio-lateral lead location, dermatomal coverage, ability to measure ECAPs, and/or paresthesia coverage of the pain areas:

- ECAP measurement - go to Section 10.4.1.
- Paresthesia mapping - go to Section 10.4.2.

10.4.1 ECAP measurement

Refer to the Evoke SCS System Clinical Manual for detailed programming instructions.

1. Connect the CI to the eCLS.
2. Check electrode impedance using the CI to ensure the leads are connected properly.
   - If electrode impedance is greater than 4000 Ω check all the connections.
   - Check impedance after each reconnection of the proximal connector to the intraoperative cable.
3. Select the stimulation and measurement electrodes and settings.
4. Verify that an ECAP can be measured by stimulating, for example, at the top and bottom of the lead.
   - If the ECAP measured is not satisfactory, change the electrodes, stimulation or measurement settings using the CI or move the percutaneous lead to a new position.
   - Verify ECAP measurement after changing settings or moving the percutaneous lead.
5. When satisfied with the lead placement, disconnect the intraoperative cable from the lead.

10.4.2 Paresthesia mapping

Refer to the Evoke SCS System Clinical Manual for detailed programming instructions.

1. Connect the CI to the eCLS.
2. Check electrode impedance using the CI to ensure the leads are connected properly.
   - If electrode impedance is greater than 4000 Ω check all the connections.
   - Check impedance after each reconnection of the proximal connector to the adapter.
3. Select the stimulation and measurement electrodes and settings.
4. Increase stimulation current until the patient reports a medium level of paresthesia (tingling).
   - Adjust settings to ensure that ECAPs are being measured correctly.
5. The patient should report paresthesia coverage of the body that aligns with their pain area.
   - If paresthesia coverage is not satisfactory, change the electrode and stimulation settings using the CI or move the percutaneous lead to a new position.

- If moving the percutaneous lead with stimulation on, enable closed-loop to automatically adjust current.
- Retest paresthesia coverage after changing settings or moving the percutaneous lead.

6. When satisfied with the lead placement, disconnect the intraoperative cable from the lead.

   Note: If the lead or lead extension will be externalized for an extended trial period, go to Section 7 'Trial with a temporary percutaneous lead' or Section 8 'Trial with a percutaneous extension' otherwise, go to Section 6 'Lead tunneling and CLS implant procedure'.

10.5 Repositioning the lead

If a lead needs to be moved the intraoperative cable may remain connected to the lead.

1. For lead steering, hold the intraoperative cable and turn the stylet handle between thumb and index finger (see Figure 10.6).
2. When the lead is in the desired location, confirm optimal lead placement (see Section 10.4).

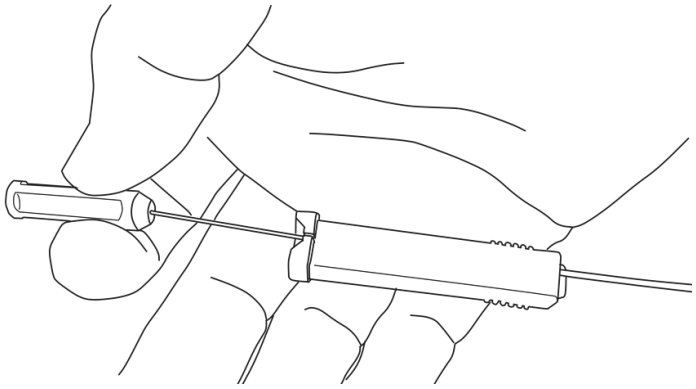


Figure 10.6: Lead steering with the intraoperative cable connected to the lead.

10.6 Disconnect the lead from the intraoperative cable

1. When satisfied with the lead placement you may disconnect the distal end of the intraoperative cable from the lead.
2. Hold the top cover between thumb and index finger of one hand and the distal end with the other hand
3. Slide the top cover off the distal end
4. Lift the lead gently out of the slot.

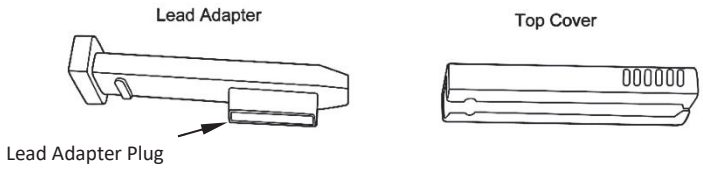
11 Preparing the eCLS for the trial stimulation period

If the patient has externalized leads or lead extensions for the purpose of a temporary trial, the externalized leads or extensions will need to be connected to the lead adapter (see Section 11.1), which in turn will need to be connected to the eCLS (see Section 11.2). The eCLS with a fully charged battery (see Section 11.4) is then placed into the eCLS case (see Section 11.3) and secured for the trial stimulation period (see Section 11.5).

11.1 Connect the lead or lead extension to the lead adapter

5. Place the tip of the proximal connector end of the lead into the end of the lead adapter slot (Figure 11.1).

A)



B)

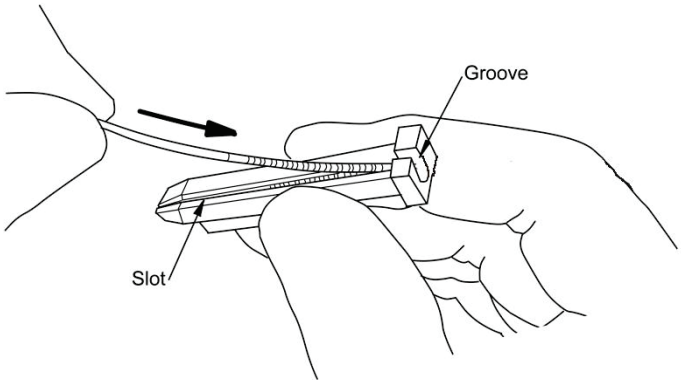


Figure 11.1: A) The lead adapter. B) Placing the tip of the proximal connector into the lead adapter slot.

6. Push the lead down into the slot completely using your finger (Figure 11.2), so that the lead is flush with the top of the slot. The lead should not move when fully pushed into the slot. After the lead is in the slot, press down again along its length to ensure it is secure in the slot.

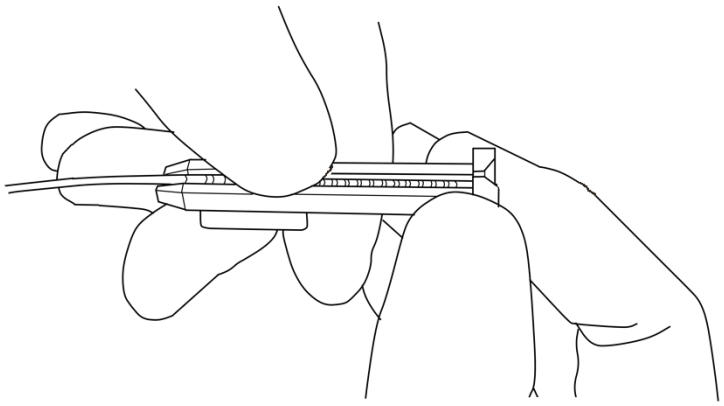


Figure 11.2: Pushing lead into lead adapter slot.

7. Place the top cover of the lead adapter over the lead, with the open side of the top cover aligned with the lead adapter plug. Slide the top cover all the way onto the lead adapter until the notch on the top cover clips into place (refer to Figure 11.3).

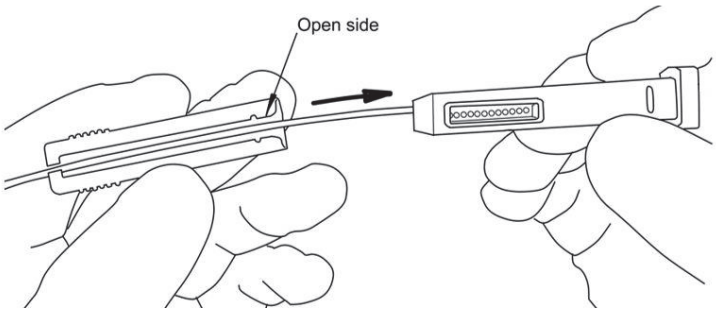


Figure 11.3: Placing the top cover over the lead and sliding onto lead adapter until it clips into place.

11.2 Connect the lead adapter to the eCLS

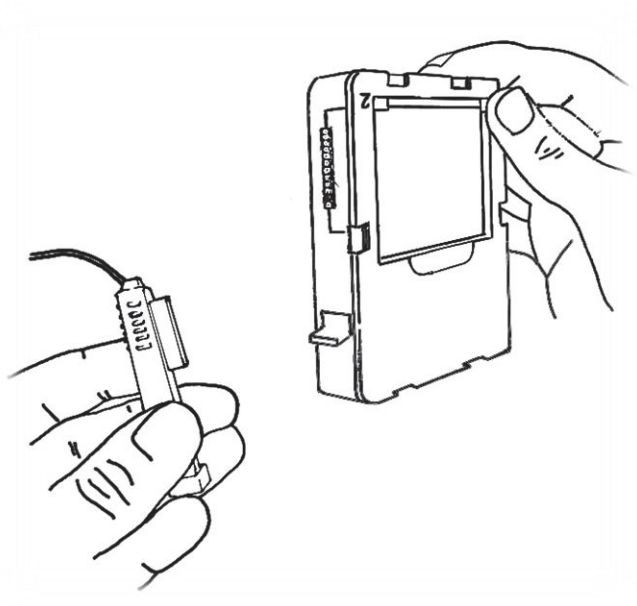


Figure 11.4: Connecting the lead adapter to the eCLS. Port 2 (electrodes 13–24) is shown here. Port 1 (electrodes 1-12) is on the opposite side of the eCLS.

1. Line up the end of the lead adapter plug with the socket on the eCLS port to ensure the connector pins do not get bent (Figure 11.4). Push the lead adapter plug into the eCLS until it clips into place.
    a. The eCLS ports are labelled ‘1’ on one side for electrodes 1-12 and ‘2’ on the other side for electrodes 13-24.

    Note: If you are reconnecting leads to an eCLS that has already been programmed, ensure that the lead and lead adapter are reinserted into the same ports as used during previous programming sessions.

2. To connect a second lead to the lead adapter, repeat the steps in Sections 11 and 11.2.

11.3 Place the eCLS into the case

1. Ensure that a fully charged battery is inserted in the eCLS (see Section 11.4; Figure 11.5).
2. Open the eCLS case with the lead exits pointing up. Place the eCLS into the orange seal side of the case, with the eCLS battery facing up and the leads pointing up over the lead exits (see Figure 11.5).
3. Place the leads into the slots in the seal at the lead exits.

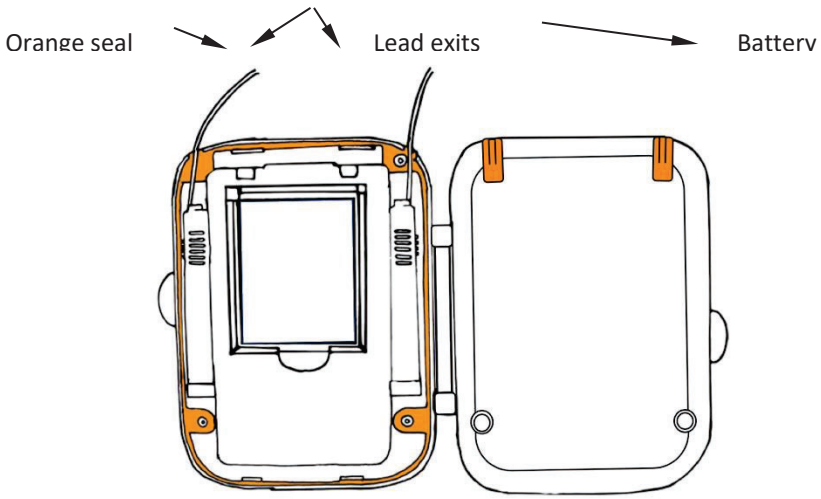


Figure 11.5: Place the eCLS with leads connected into the eCLS Case.

4. Close the eCLS case by folding the case shut until it snaps closed (Figure 11.6). Ensure that the leads do not move from the slots in the seal. The leads may be damaged when the case is closed if they are not in the slots in the seal at the lead exits.



Figure 11.6: eCLS with two leads connected enclosed in case.

5. After the eCLS is connected and in the eCLS case it may be programmed (refer to Evoke SCS System Clinical Manual) and set up for the patient to wear for the trial stimulation period (see Section 11.5).

11.4 Charge the eCLS battery

1. Before the patient goes home with an eCLS, a fully charged eCLS battery should be in place (see Figure 11.5).
2. Check the battery voltage with the CPA (refer to Evoke SCS System Clinical Manual).
3. To charge the eCLS battery:
    a. Disconnect the intraoperative cables or lead adapters from the eCLS.

   b. Remove the battery from the eCLS.
   c. Charge the battery using the supplied eCLS battery charger.
4. Place the charged battery into the eCLS
5. Connect intraoperative cables or lead adapters to the eCLS.

11.5 Secure the eCLS for the trial stimulation period

1. The eCLS may be worn by the patient for the duration of the trial stimulation period in either of two ways:
   a. In a pouch (see the Accessory Belt section in the Evoke SCS System User Manual), or
   b. Placed on a dressing and taped to the skin by the clinician.
2. The eCLS and leads remain connected inside the eCLS case during the trial stimulation period. If the leads become disconnected from the eCLS or the patient needs to disconnect the eCLS for any reason the patient should return to the clinic.

12 Sterilization

All items detailed in this document, with the exception of the eCLS, EPC, Charger and Accessory Belt, are provided sterile and are for single use only. None of these items should be re-sterilized or reused. Sterilization method is Ethylene Oxide.

DO NOT STERILIZE the eCLS, EPC or Charger. These devices are external system components that do not require sterilization. Clean these components regularly as detailed in Section 15 ‘Maintenance of the Evoke eCLS, EPC, and Charger’.

13 Patient ID card

Every CLS is supplied with a Patient ID Card for the clinician to complete.

- Give the completed Patient ID Card to the patient so that they can use it to show other medical practitioners or security personnel that they have an active implanted medical device.
- Educate the patient to show the Patient ID card to healthcare professionals before undergoing any medical procedure.
- The Patient ID Card indicates that the Evoke System is MR Conditional in certain system configurations, under specific scanning parameters. The card advises the patient to inform their physician if an MRI is being considered and to refer to the MRI clinical staff to the Evoke SCS System MRI Guidelines accessible at https://www.saludamedical.com/manuals.

14 Identifying the Evoke CLS

Prior to implantation, the serial number of the CLS can be located on the surface of the CLS. Following implantation, the serial number of the CLS can be found on the patient's ID Card, or can be identified using the Clinical Programming Application, in communication with the CLS.

The CLS can also be identified by a radiopaque marker, which can be viewed by standard x-ray procedures. The radiopaque characters consist of a code in the following format: SME DYY, where SME indicates Saluda Medical, D indicates the CLS model, and YY indicates the two-digit year of manufacture. The radiopaque marker can be used to confirm the MR compatibility of an implanted CLS without surgical intervention. Refer to the Evoke SCS System MRI Guidelines for information on the MR compatibility of the Evoke SCS System.

15 Maintenance of the Evoke eCLS, EPC, and Charger

The eCLS, EPC, and Charger are designed to be used by multiple patients during a temporary trial stimulation period, and so should be cleaned thoroughly between patients. The devices can be cleaned with a soft cloth dampened with a mild disinfectant or alcohol.

⚠ **Caution:** The battery must be removed from the eCLS prior to cleaning.

Do not use abrasive cleaners and avoid wiping the connectors on the Charger and eCLS, if applicable.

DO NOT STERILIZE the eCLS, EPC or Charger. These items are supplied non-sterile. Sterilization could damage these components beyond repair and impact their ability to perform as intended.

The eCLS is supplied with a replaceable, rechargeable battery with a dedicated battery charger. Please refer to Section 11.4 for instructions on eCLS battery recharging.

16 Package contents

Table 16.1: Package contents.

Package	***Package Contents***
Evoke Closed-Loop Stimulator **(Ref No.: 3002 or 3042)**	1 x Evoke Closed-Loop Stimulator 1 x Evoke CLS Port Plug 1 x Torque Wrench
Evoke External Closed-Loop Stimulator **(Ref No.: 3036)**	1 x Evoke External Closed-Loop Stimulator
Evoke eCLS Case **(Ref No.: 3035)**	1 x Evoke eCLS Case 2 x Lead Adapters 2 x Top Covers

Package	*Package Contents*
Evoke CAP12 Percutaneous Lead Kit - 60 cm (Ref No.: 3008*) **Evoke CAP12 Percutaneous Lead Kit - 90 cm (Ref No.: 3009*)** **Evoke CAP12 Trial Lead Kit - 60cm (Ref No.: 3016*)** **Evoke CAP12 Trial Lead Kit - 90cm (Ref No.: 3017*)**	1 x Evoke CAP12 Percutaneous Lead, 1 x Evoke Suture Anchor 1 x Epidural Needle, 14-gauge, 11.3 cm (4.5 in) spoonbill type. 1 x Bent Stylet (15° angle) of 0.36 mm (0.014 in) diameter (preloaded in lead). 1 x Straight Stylet of 0.36 mm (0.014 in) diameter.
Evoke CAP12X Lead Extension Kit – 55 cm (Ref No.: 3011*)	1 x Evoke CAP12X Lead Extension 1 x Torque Wrench
Evoke Active Anchor Kit (Ref No.: 3043*)	2 x Evoke Active Anchor 1 x Torque Wrench
Evoke Active Anchor Kit – L (Ref No.: 3043)	2 x Evoke Active Anchor 1 x Torque Wrench (Long)
Evoke Tunneler (Ref No.: 3012*)	1 x Tunneler (with passing straw and tip protector).
Evoke Intraoperative Cable Kit (Ref No.: 3034)	1 x Intraoperative Cable 1 x Top Cover
Epidural Needle, 6.5” (Ref No.: 3014)	1 x Epidural Needle, 14-gauge, 16.5 cm (6.5 in) spoonbill type.

Package	*Package Contents*
Evoke Spares Kit (Ref No.: 3015*)	2 x Evoke Suture Anchors 1 x Epidural Needle, 14-gauge, 11.3 cm (4.5 in) spoonbill type. 1 x Bent Stylet (15° angle) of 0.36 mm (0.014 in) diameter, compatible with 90 cm Percutaneous Lead. 1 x Straight Stylet of 0.36 mm (0.014 in) diameter, compatible with 90 cm Percutaneous Lead. 1 x Bent Stylet (15° angle) of 0.36 mm (0.014 in) diameter, compatible with 60 cm Percutaneous Lead. 1 x Straight Stylet of 0.36 mm (0.014 in) diameter, compatible with 60 cm Percutaneous Lead. 1 x Torque Wrench 1 x Evoke CLS Port Plug
Evoke Accessory Belt **(Ref No.: 3039)**	1 x Evoke Accessory Belt

*** Note:** Consult CLIN-UMAN-005177 Rev. 7.00 for original packaging configurations.

17 Technical Specifications

17.1 Evoke SCS System Components

Table 17.1: Evoke SCS System Components.

Ref Number	*Product Description*
3002 or 3042	Evoke Closed-Loop Stimulator (CLS)
3040	Evoke Patient Controller
3004	Evoke Clinical System Transceiver (CST)
3006	Evoke Charger (US)
3008	Evoke CAP12 Percutaneous Lead Kit - 60cm

Ref Number	***Product Description***
3009	Evoke CAP12 Percutaneous Lead Kit - 90cm
3011	Evoke CAP12X Lead Extension Kit - 55cm
3043	Evoke Active Anchor Kit
	Evoke Active Anchor Kit – L
3012	Evoke Tunneler
3014	Evoke Epidural Needle, 6.5"
3015	Evoke Spares Kit
3016	Evoke CAP12 Trial Lead Kit - 60cm
3017	Evoke CAP12 Trial Lead Kit - 90cm
3036	Evoke External Closed-Loop Stimulator (eCLS)
3035	Evoke eCLS Case
3024	Clinical Interface (CI)
3034	Evoke Intraoperative Cable Kit
3039	Evoke Accessory Belt Kit

17.2 Device Specifications

Refer to the Evoke SCS System Clinical Manual and Evoke SCS System User Manual for device specifications for additional components of the Evoke SCS System.

17.2.1 Evoke CLS (REF 3002)

Table 17.2: Evoke CLS (REF 3002)

Materials	Case	Titanium
	Header	Epoxy
	Seals	Liquid silicone rubber
	Connector springs	Platinum Iridium (24 x connectors)
	Set screw	Stainless steel
Dimensions	68 mm x 48 mm x 12 mm (2.7 in x 1.9 in x 0.472 in)	
Volume	33 cm^3 (2 in^3)	
Weight	50 g (1.76 oz.)	
Lead ports	2	Each lead is secured by a set screw at the port entry
Electrodes	25	Port 1: electrodes 1-12 Port 2: electrodes 13-24 CLS case is electrode 25 (recording only)
Stimulation parameters	Current	0 mA – 50mA (20 mA @750 Ω)
	Pulse Width	20 µs – 1000 µs
	Frequency	10 Hz – 1400 Hz
Radio frequency communication	MICS band	402-405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	
		300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	
		25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3002

*Channels are automatically selected when the communication session begins.

Battery	Battery type	200 mAh Li-Ion rechargeable battery	
	Battery life	Greater than 10 years at moderate settings (current = 5.0 mA, pulse width = 200 µs, frequency = 60 Hz, impedance = 750 Ω, 24hrs/day usage)*	
*End of Battery Life is defined by Saluda Medical as the point at which the device can no longer maintain enough charge to provide 24hrs of therapy. At higher or lower settings this defined end of life could be shorter or longer respectively			
Charging	Transcutaneous charging using inductive coupling with an external coil		
	Implant depth	5 mm to 20 mm (0.2 in to 0.8 in)	
Recording amplifier gain	Low: 250x High: 1000x		
Data recording	32 MB, up to 1 year (Stimulation usage, ECAP amplitude and current statistics)		
Radio opaque identifier	"SME BYY" Where "SME" is Saluda Medical, "B" is the CLS model and YY is the two-digit year of manufacture		
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)

17.2.2 Evoke CLS (REF 3042)

Table 17.3: Evoke CLS (REF 3042)

Materials	Case	Titanium
	Header	Epoxy
	Seals	Liquid silicone rubber
	Connector springs	Platinum Iridium (24 x connectors)
	Set screw	Stainless steel
Dimensions	67.5 mm x 47.7 mm x 11 mm (2.65 in x 1.88 in x 0.43 in)	
Volume	32.6 cm^3 (2 in^3)	
Weight	49 g (1.73 oz.)	
Lead ports	2	Each lead is secured by a set screw at the port entry
Electrodes	25	Port 1: electrodes 1-12 Port 2: electrodes 13-24 CLS case is electrode 25 (recording only)
Stimulation parameters	Current	0 mA – 50mA (20 mA @750 Ω)
	Pulse Width	20 µs – 1000 µs
	Frequency	10 Hz – 1400 Hz
Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3042
*Channels are automatically selected when the communication session begins.		
Battery	200 mAh Li-Ion rechargeable battery	
Battery life	Greater than 10 years* at moderate settings (current = 5.0 mA, pulse width = 200 µs, frequency = 60 Hz, impedance = 750 Ω, 24hrs/day usage) Greater than 10 years* for more than 95% of patients	

*End of CLS Battery Life is defined by Saluda Medical as the point at which the device can no longer maintain enough charge to provide 24hrs of therapy. At higher or lower settings this defined end of life could be shorter or longer respectively

Charging	Transcutaneous charging using inductive coupling with an external coil Implant depth	5 mm to 20 mm (0.2 in to 0.8 in)	
Recording amplifier gain	Low: 250x High: 1000x		
Data recording	32 MB, up to 1 year (Stimulation usage, ECAP amplitude and current statistics)		
Radio opaque identifier	"SME EYY" Where "SME" is Saluda Medical, "E" is the CLS model and YY is the two-digit year of manufacture		
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)

17.2.3 Evoke eCLS (includes Case and Lead Adapters)

Table 17.4: Evoke eCLS.

Materials	eCLS body and case	ABS Plastic
	Case Seal	TPE
Dimensions	100 mm x 85 mm x 20 mm (3.9 in x 3.4 in x 0.8 in)	
Weight	96 g (3.4 oz.)	
Electrodes	24	Port 1: electrodes 1-12, Port 2: electrodes 13-24
Functional specifications	All other functional specifications are the same as the CLS (See Section 17.2.1)	
Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Range	1.0 m (3.3 ft.)
	Effective Isotropic Radiated Power (EIRP)	25 µW (-16.02 dBm) maximum
	FCC ID	2AYGR-3036
*Channels are automatically selected when the communication session begins.		
Battery	800 mAh Li-ion 3.6 V rechargeable battery	
Battery Life	Greater than 14 days between charges at moderate settings.	
	Greater than 7 days between charges for more than 95% of patients.	
Charging	Li-Ion battery charger	
Ingress Protection eCLS in case	IP22 Rating for protection against access of solid objects greater than or equal to 12.5mm, and for vertically dripping water when the device is tilted 15 degrees.	
eCLS	IP30 Rating for protection against solid objects greater than or equal to 2.5mm, and no protection against water.	
IEC 60601-1 / EN 60601-1 Classification	Type BF Applied Part Internally Powered Medical Electrical Equipment Continuous Operation	

Storage & Transportation Conditions	Temperature: Humidity: Pressure:	Min: -10 °C (14 °F) Min: 0% RH 70kPa (0.69 atm)	Max: 55 °C (131 °F) Max: 90% RH Max: 106kPa (1.05 atm)
Operating Conditions	Temperature: Humidity: Pressure:	Min: 5 °C (41 °F) Min: 15% RH 70 kPa (0.69 atm)	Max: 40 °C (104 °F) Max: 90% RH Max: 106 kPa (1.05 atm)

Table 17.5: Lead Adapter.

Materials	Body	ABS Plastic
Dimensions	55 x 13 x 13 mm (2.2 x 0.5 x 0.5 in)	
Lead connection	Ports 12 spring connectors	1 Au plating on stainless steel
Lead Adapter to eCLS connection	12 pin plug	

17.2.4 Evoke CAP12 Percutaneous Lead (includes Trial Leads)

Table 17.6: Evoke CAP12 Percutaneous Lead (includes Trial Leads).

Materials	Lead body	Pellethane	
	Lead ends	Pellethane	
	Distal electrodes	Platinum Iridium	
	Proximal connectors	Platinum Iridium	
	Retention ring	MP35N[1]	
	Conductors	35N LT with Ag core (19 strand cable)	
Dimensions	Lengths	60 cm (1.97 ft.) or 90 cm (2.95 ft.)	
	Diameter	1.32 mm (0.05 in)	
Electrodes	Number	12	
	Length	3 mm (0.12 in)	
	Pitch	7 mm (0.276 in)	
Connectors	Length	1.02 mm (0.040 in)	
	Pitch	1.96 mm (0.077 in) center to center	
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)
	[1] Alloy of Nickel, Cobalt, Chromium and Molybdenum. MP35N is not in contact with tissue, but may be in contact with body fluid.		

17.2.5 Evoke CAP12X Lead Extension

Table 17.7: Evoke Lead Extension.

Materials	Lead extension body	Pellethane	
	Lead extension ends	Pellethane	
	Proximal connectors	Platinum Iridium	
	Retention ring	MP35N[1]	
	Connector springs	Platinum Iridium	
	Set screw	Titanium	
	Header body	Silicone	
Dimensions	Length	55 cm (1.8 ft.)	
	Body Diameter	1.32 mm (0.05 in)	
	Header Length	41 mm (1.62 in)	
	Header Diameter	5.45 mm (0.21 in)	
Connectors	Number	12	
	Length	1.02 mm (0.040 in)	
	Pitch	1.96 mm (0.077 in) center to center	
Storage & Transportation Conditions	Temperature:	Min: -10 °C (14 °F)	Max: 55 °C (131 °F)
Operating Conditions	Pressure:	70 kPa (0.69 atm)	Max: 150 kPa (1.48 atm)
	[1] Alloy of Nickel, Cobalt, Chromium and Molybdenum. MP35N is not in contact with tissue, but may be in contact with body fluid.		

17.2.6 Surgical accessories

Table 17.8 below lists the specifications for the surgical accessories found in the various component kits as detailed in Section 16 ‘Package contents’.

Transport and store surgical accessories at temperatures from -10 °C (14 °F) to 55 °C (131 °F). Operate surgical accessories at pressures from 70kPa (0.69 atm) to 106kPa (1.05kPa).

Table 17.8: Surgical Accessories.

Epidural Needle	**Material**	Stylet and Cannula	Stainless Steel
		Hub and Cap	Nickel-plated Brass
	Dimensions	Lengths	113 mm (4.5 in) and 165 mm (6.5 in)
		Diameter	14 gauge (1.74 mm internal)
Stylet	**Forms**	Straight or bent (15° angle)	
	Material	Body	Stainless steel
		Stylet hub	ABS Plastic
	Dimensions	Length	To suit each electrode length
		Diameter	0.356 mm (0.014 in)
Suture Anchor	**Form**	Two suture eyelets	
	Material	Silicone rubber	
	Diameter	5 mm (0.20 in)	
	Length	34 mm (1.34 in)	
Active Anchor	**Form**	Three suture eyelets, and a set screw to secure the lead	
	Materials	Body	Silicone rubber
		Set screw	Titanium
		Set Screw Block	Titanium
	Height	6.7 mm (0.26 in)	
	Length	34.2 mm (1.35 in)	
Tunneler	**Materials**	Body	Stainless steel
		Straw	PTFE
	Dimensions	Length	279.4 mm (11 in)
		Straw length	203.2 mm (8 in)
		Body diameter	4 mm (0.157 in)
		Straw ID	4.22 mm (0.166 in)
		Straw OD	4.60 mm (0.181 in)

Torque Wrench	**Materials**	Handle	Polyetherimide plastic
		Shaft	Stainless steel
	Dimensions	Length	43 mm (1.69 in) or 76.5 mm (3.01 in)
		Bit size	0.9 mm (0.035 in) hex key
	Torque	0.042 Nm (6 oz-in)	
CLS Port Plug	**Materials**	Stainless steel	
	Length	13 mm (0.51 in)	
Intra-operative Cable	**Materials**	Socket	ABS Plastic
		Plug	ABS Plastic
		Cable	TPE
	Dimensions	Socket	55 x 13 x 13 mm (2.2 x 0.5 x 0.5 in)
		Plug	62.5 x 19.8 x 14.5 mm (2.5 x 0.8 x 0.6 in)
	Cable Length	2.5m (8 ft. 2.4 in)	
	Lead Connection	Ports	1
		12 spring connectors	Au plating on stainless steel
	eCLS Connection	12 pin plug	

17.3 Wireless Communication

17.3.1 Quality of Service & Wireless Coexistence

The Evoke SCS System employs a wireless communication link operating in the 402-405 MHz MICS frequency band. This band is designated for implantable medical devices and enables communication between the CLS/eCLS and the CST or EPC.

At the beginning of each communication session, the CST or EPC automatically scans 8 channels in the frequency band and selects the least congested channel for communication. All communication is error-checked. The user is notified if the wireless communication link fails to connect.

The communication range between the CST/EPC and the CLS/eCLS is typically 3.3 feet (1 meter). If you experience issues with the wireless communication between the CST/EPC and CLS/eCLS, try the following:

- Decrease the distance between the devices.
- Move the devices away from other devices that may be causing interference (see Section 17.4).
- Restart the CPA, wait a few minutes and try connecting again.
- Do not operate other wireless devices, such as a mobile phone, tablet or laptop, at the same time.

17.3.2 Wireless Security

The Evoke SCS System has a communication range of 3.3 feet (1 meter). To enable the CST/EPC to communicate with an eCLS or CLS, it must first be paired with that stimulator. The CST/EPC may communicate with only one CLS or eCLS at a time. The stimulator will not respond to any communication that does not come from a paired device. Additional mechanisms are in place to safeguard the integrity of the communication. There are no security settings that require input or control by the user.

17.4 Electromagnetic Interference

The following tables indicate the electromagnetic environment in which the Evoke SCS System is intended to operate. This is to ensure compliance with international standards for the electromagnetic interference (EMI) produced by the Evoke SCS System or the susceptibility of the Evoke SCS System to EMI. For more information on this section please contact a Saluda Representative.

⚠**Caution:** Use of accessories, transducers, and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

17.4.1 Guidance and Manufacturer's Declarations

Table 17.9: Electromagnetic emissions.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.		
Emissions Test	**Compliance**	**Electromagnetic environment – guidance**
Radiated disturbance, 30 MHz -6000 MHz CISPR 11 (EN 55011)	Group 1, Class B	Evoke SCS System is unlikely to produce electromagnetic interference with nearby electronic equipment.
Conducted Emissions 0.15 MHz -30 MHz CISPR 11 (EN 55011)	Class B	Evoke SCS System is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable for the battery powered devices or device consuming less than 75 W from mains power outlet (Charger with power adapter)	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Not applicable for the battery powered devices. Charger with power adapter complies with requirements of the standard	

Table 17.10: Electromagnetic immunity – electrostatic discharge and mains power.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.			
Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic environment – guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV air	±2 kV, ±4 kV, ±6 kV, ±8 kV contact ±2 kV, ±4 kV, ±8 kV, ±15 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%
Electrical fast transient/burst IEC 61000-4-4	± 2 kV gaseous discharge at 100 kHz repetition frequency	± 2 kV @100 kHz repetition frequency for power supply lines to Charger power adapter	Mains power quality should be that of a typical household, commercial or hospital environment. If the user of the Charger power adapter requires continued operation during mains power interruptions, it is recommended that the Charger power adapter be powered from an uninterruptible power supply or a battery.
Surge Immunity IEC 61000-4-5	± 0.5 kV, ± 1 kV	± 0.5 kV, ± 1 kV power supply line to Charger power adapter	
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0 % residual voltage; 1 cycle, and 70 % residual voltage; 25/30 cycles Single phase: at 0° Voltage Interruptions: 0% residual voltage; 250/300 cycles	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0% residual voltage for 1 cycle at 0 °; 70% residual voltage for 25 cycles at 0 °; Voltage Interruptions: 0% residual voltage for 250 cycles at 0 °; Interval between Events – min. 10s; Test cycle – 3 times;	
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m 50/60 Hz	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical household, commercial or hospital environment.

Table 17.11: Electromagnetic immunity – radio frequency.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.

⚠**Caution:** Portable and mobile RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer to any part of the Evoke SCS System, including cables, than the recommended separation distance stated below (0.3 m, 12 inches). Otherwise, degradation of the performance of this equipment could result.

⚠**Caution:** Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic environment – guidance**
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz; 6 Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz 80% AM at 1 kHz	The Charger power adaptor functioned correctly during the test. Not applicable for the battery powered devices.	The separation distance between an interfering RF transmitter and any Evoke SCS should be greater than 0.3 m and the maximum power from the RF transmitter should not exceed 2 W or 28 V/m at a distance of 0.3 m.
Radiated RF IEC 61000-4-3	10 V/m 80 MHz to 2.7 GHz 80% AM at 1 kHz	3 V/m for professional healthcare facility environment or 10 V/m for home healthcare environment	
Proximity fields from RF wireless communications equipment	Up to 28 V/m at 0.3m at specified frequencies (refer Table 9, IEC 60601-1-2)	Tested at up to 28 V/m, devices continued to function during test.	

17.5 Federal Communications Commission (FCC)

17.5.1 Interference Statement for CLS, eCLS and EPC

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable

protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
- Consult the dealer or an experienced radio/TV technician for help.

⚠**FCC Caution:** Any changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate this equipment.

This transmitter must not be co-located or operating in conjunction with any other antenna or transmitter.

The devices in the Evoke System may not interfere with stations operating in the 400.150 - 406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

For MedRadio transmitters operating in the 401-406 MHz band, the following statement applies:

> This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

17.5.2 Charger

This device complies with Part 18 of the FCC Rules.

17.5.3 Radiation Exposure Statement

The products comply with the FCC portable RF exposure limit set forth for an uncontrolled environment and are safe for intended operation as described in this manual.

18 Glossary

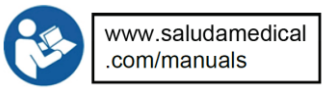
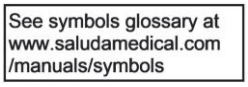
Table 18.1: Glossary.

Term	Definition
Accessory Belt	An elastic belt with a pouch to hold an eCLS or a Charger coil.
Charger	The device that charges the battery in the CLS.
Charger coil	A circular paddle connected to the Charger that is held over the CLS to charge the CLS battery.
Charger Power Adapter	The power supply adapter for the CLS Charger.
Clinical Interface (CI)	The computer loaded with the CPA used to program the CLS/eCLS.
Clinical System Transceiver (CST)	The device that connects to the CI via USB, and exchanges information between the CI and the CLS/eCLS.
Clinical Programming Application (CPA)	A computer program user interface that provides the functionalities required to program and analyze the performance of the CLS/eCLS.
Closed-Loop (CL) Stimulation (see also PCLC below)	Stimulation that is automatically adjusted in response to a measured ECAP amplitude to maintain a target activation level. This is also known as ECAP-controlled closed-loop stimulation.
Closed-Loop Stimulator (CLS)	An implantable pulse generator capable of ECAP-controlled closed-loop stimulation.
Electrode	An electrical contact that may be employed to deliver therapeutic current or measure neural responses.
Evoke Patient Controller (EPC)	A remote control that allows the patient to adjust the therapy output from the CLS/eCLS.
Evoked Compound Action Potential (ECAP)	The measured sum of electrical signals from multiple nerve fibers elicited by an electrical stimulus.
External Closed-Loop Simulator (eCLS)	The eCLS is a non-implantable pulse generator capable of ECAP-controlled closed-loop stimulation.
Intraoperative Cable	Sterilized cable which enables the connection between leads/lead extensions and the eCLS in the operating room.
Lead	Insulated cable with a number of exposed electrodes at the distal end used in neurostimulation therapy.

Term	Definition
Lead Adapter	An adapter that enables the connection between leads/lead extensions and the eCLS during the trial stimulation period.
Lead Extension	Insulated cable that connects to the proximal end of a lead and in turn connects to a lead adapter.
Open-Loop Stimulation	Stimulation delivered when closed-loop is disabled. The system delivers a fixed-output of stimulation current when closed-loop stimulation is disabled.
Paresthesia	Sensation felt by the patient as a result of activation of Aβ fibers by the stimulation pulses.
Physiologic Closed-Loop Controlled (PCLC) Stimulation	Stimulation that is automatically adjusted in response to a measured ECAP amplitude to maintain a target activation level. This is also known as ECAP-controlled closed-loop stimulation.
Spinal Cord Stimulation (SCS)	A treatment for chronic pain utilizing pulsed electrical signals delivered to the spinal cord.
Stimulation	The application of electrical current through electrodes.

19 Symbols

Table 19.1: Symbols.

Symbol	Definition
	Follow the instruction for use on this website: www.saludamedical.com/manuals
	Follow the instructions for use
	Follow the instructions for use at this website: www.saludamedical.com/manuals
	Symbols Glossary can be found on this website: www.saludamedical.com/manuals/symbols
	Catalogue number
	Serial number
	Lot number

Symbol	Definition
 YYYY-MM-DD	Use by date (YYYY = year, MM = month, DD = day)
	Caution
	Temperature limitation (°F and °C)
	Manufacturer
 YYYY-MM-DD	Date of manufacture (YYYY = year, MM = month, DD = day)
	Do not dispose of this product in the unsorted municipal waste stream – dispose of this product according to local regulations
	Type BF applied part
	Non-ionizing electromagnetic radiation
	Do not use if package is damaged
	MR Conditional: Refer to Evoke SCS System MRI Guidelines at https://www.saludamedical.com/manuals
	Magnetic Resonance (MR) unsafe. External components of the Evoke SCS System are MR Unsafe.
	Contents
	Class II Medical Electrical Equipment
IP22	Ingress Protection Rating 22: • Protected against access of solid foreign objects greater than or equal to 12.5 mm diameter. • Protected against vertically dripping water when the device is tilted 15 degrees.

Symbol	Definition
IP30	Ingress Protection Rating 30: • Protected against solid objects greater than or equal to 2.5 mm, and no protection against water.
IP54	Ingress Protection Rating 54: • Protected against failure from limited dust ingress. • Protected against failure from splashing water.
	Sterilized using ethylene oxide
	Do not re-sterilize
	Do not re-use
	Single Sterile Barrier System with an additional packaging layer inside
	Single Sterile Barrier System with an additional packaging layer inside
	Double Sterile Barrier System
	Double Sterile Barrier System
Rx Only	Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner
	Peel open from here
	Telephone Number

20 Disposal of devices

Neither the CLS nor the eCLS should be disposed of in municipal waste facilities. Please return any items to Saluda Medical via your Saluda Medical representative for proper disposal. Surgical accessories should be disposed of in accordance with normal clinical practices.

21 Contact us

Most questions you have about programming the Evoke Closed-Loop Stimulator and Evoke External Closed-Loop Stimulator can be answered by reading this manual or looking at our website: https://www.saludamedical.com and/or https://www.saludamedical.com/manuals.

If you have any further questions, please contact your Saluda Medical representative. Alternatively, you can contact us via the details below, or email us at info@saludamedical.com.

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Evoke® SCS System Clarity™ Clinical Manual

For Clarity Version 2.0

Use of the Evoke Clinical Interface (CI) and Clarity Programming Application (CPA) with the Evoke Clinical System Transceiver (CST) for programming the Evoke SCS System

Rx Only

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Refer to the Evoke SCS System Surgical Guide for:

- System warnings and precautions
- Instructions on the implantation of the Evoke System components
- Other system component device specifications and package contents

Refer to the Evoke SCS System User Manual for:

- Instructions on the use of the Evoke Patient Controller (EPC), Magnet, Accessory Belt and Evoke Charger.

Refer to the Evoke SCS System MRI Guidelines for information on the safe use of the Evoke System in the MRI environment.

Manuals are accessible at https://www.saludamedical.com/manuals.

1. Description

The Saluda® Medical Evoke® SCS System is a Spinal Cord Stimulation (SCS) system that incorporates ECAP-controlled closed-loop stimulation for the management of chronic, intractable pain. The Evoke System measures evoked compound action potentials (ECAPs) and may be programmed to deliver either ECAP-controlled closed-loop SCS or fixed-output open-loop SCS.

The Evoke Clinical Interface (CI) and Evoke Clinical System Transceiver (CST) enable the programming of the implantable Closed-Loop Stimulator (CLS) and the non-implantable External Closed-Loop Stimulator (eCLS).

The Evoke System may be used in conjunction with other pain management therapies, as determined by the physician.

1.1 The concept of ECAP-controlled physiologic closed-loop SCS

The Evoke System uses ECAP amplitude to measure the patient's neural response and provide physiologic closed-loop controlled SCS. The ECAP amplitude is a measure of the spinal cord activation or number of dorsal column fibers in the spinal cord that are activated by a stimulation pulse. When closed-loop (CL) is enabled, the system automatically varies the stimulation current for every pulse to maintain consistent spinal cord activation during physiological changes and movement.

Figure 1.1, below, depicts the concept of a physiologic closed-loop controlled system using ECAPs. Following a stimulation pulse, the amplitude of the ECAP that is generated in the spinal cord by that stimulus is recorded. The ECAP amplitude is compared to the selected target and then used to automatically adjust the current of the next stimulus to maintain a consistent ECAP amplitude.

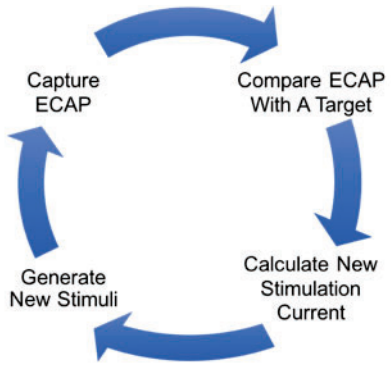


Figure 1.1: ECAP-Controlled Closed-Loop SCS.

1.2 Stimulation Features

The Evoke System provides the following advanced stimulation options.

1.2.1 Closed-loop SCS

When closed-loop is enabled, the system uses feedback of the ECAP amplitude to automatically adjust the stimulation current of every pulse to maintain a target activation level. This ensures consistent dorsal column activation during physiological changes and movement.

1.2.2 Open-loop SCS

When closed-loop is disabled, the system delivers a fixed-output of stimulation current, while continuing to measure ECAP amplitude. Since the stimulation current is fixed, the activation level will vary as the spinal cord moves relative to the stimulation electrodes.

1.2.3 Current steering

Multiple stimulation electrodes can be used simultaneously, with a scaled portion of the total current delivered to each electrode. This enables more targeted stimulation between electrodes.

1.2.4 Interleaved stimulation

Two or more stimulation configurations can be used concurrently, with the system automatically cycling through each configuration. Each interleaved configuration (Stim-Set) can target a different area of the patient's pain.

1.2.5 Stimulation Waveform

Each stimulation waveform consists of constant current, actively charge-balanced, pulses. The output current is automatically controlled when closed-loop is enabled and set to a fixed level when closed-loop is disabled. The stimulation waveform can be customized (see Figure 1.1 for example) by the selection of the following parameters: pulse shape, polarity, stimulation current, and pulse timing.

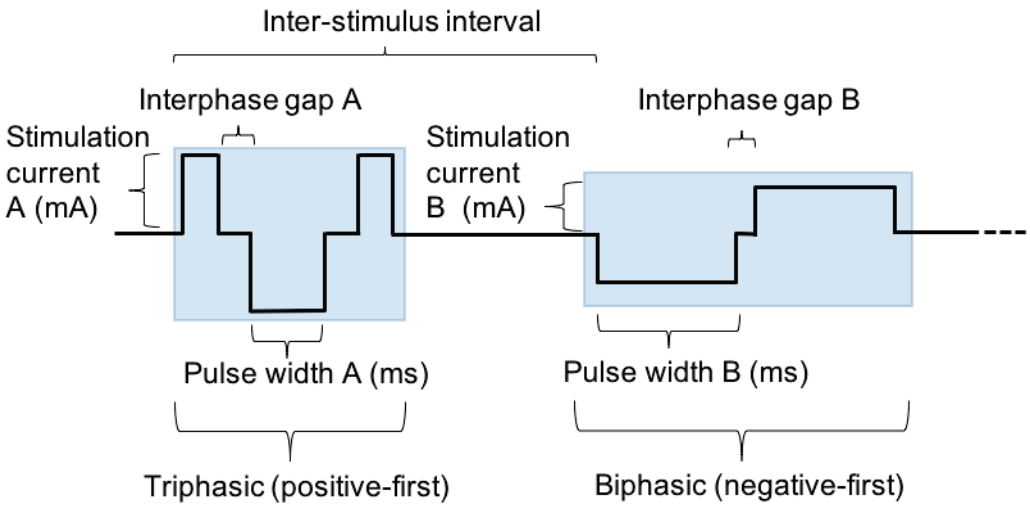


Figure 1.2: Example stimulation waveform for a program with two Stim-Sets. Stim-Set A is shown with triphasic and positive-first, and Stim-Set B is shown with biphasic and negative-first. Each Stim-Set may also have a different stimulation current, pulse width, and interphase gap. The inter-stimulus interval is configurable for each program.

1.2.5.1 *Pulse shape and polarity*

Each pulse can be configured to have two (biphasic) or three (triphasic) phases, and to either start with a positive phase (positive-first) or negative phase (negative-first). The pulse shape and polarity can be customized for each Stim-Set (see Section 6.4.4 to set the pulse shape and polarity, and Figure 1.2 for examples).

1.2.5.2 *Stimulation current*

When closed-loop is disabled, the stimulation current is fixed at the level chosen by the user (see Section 6.4.4). When closed-loop is enabled, the stimulation current is automatically adjusted in response to the difference between the ECAP amplitude and the target level chosen by the user. The stimulation current can be customized for each Stim-Set, such that the ratio of stimulation currents between each Stim-Set is kept constant.

1.2.5.3 *Pulse width*

With a biphasic pulse, the pulse width sets the duration of each phase. With a triphasic pulse, the pulse width sets the duration of the second phase, which is equal to the sum of the durations of the first and third phase. The pulse width can be customized for each Stim-Set (see Section 6.4.4).

1.2.5.4 *Interphase gap*

The interphase gap is a pause between each phase when no current is delivered (e.g. Figure 1.2). The interphase gap can be customized for each Stim-Set (see Section 6.4.4).

1.2.5.5 *Inter-stimulus interval*

In programs with 2 to 4 Stim-Sets (see Section 6.4.4.2), the inter-stimulus interval sets the time between the start of the pulses from one Stim-Set and the start of the next Stim-Set (e.g. Figure 1.2). The inter-stimulus interval can be customized for each program (see Section 6.4.4). In programs with one Stim-Set, this parameter is not used.

1.2.5.6 *Stimulation Frequency*

Each stimulation waveform as defined by the above parameters (e.g. Figure 1.2.) repeats at a set frequency. The stimulation frequency can be customized for each program (see Section 6.4.4).

1.3 Measurement Features

The Evoke System supports the following types of measurements and data analysis. Refer to the Evoke SCS System RECAP Viewer User Manual for additional information on data analysis.

1.3.1 ECAP Measurements

ECAP amplitude is a measure of spinal cord activation and is used by the stimulator for closed-loop stimulation. ECAP signals can be viewed in the CPA during a programming session (to objectively observe the patient's neural response, independent of the patient's subjective reports), and also later analyzed in the RECAP Viewer for their objective features (such as shape, latency, conduction velocity and amplitude).

1.3.2 ClearCAP™

ClearCAP is used to reduce the artefact recorded during measurement by cancelling the artefact from the stimulation and return electrodes; this feature is best used when optimizing ECAP measurement (see Section 6.4.5).

1.3.3 Therapeutic window

During a programming session, the CPA may be used to record the ECAP amplitude at the patient's threshold, comfort and maximum levels, which may then be used to define the patient's therapeutic window.

1.3.4 Detection of late response

Late responses are neural responses resulting from dorsal root activation. Late responses have longer latency than ECAPs and they do not propagate along the spinal cord. They can be viewed in the CPA during a programming session or reviewed later in the RECAP Viewer.

1.3.5 Activation Plot and Sensitivity

The CPA displays a plot of activation (ECAP amplitude) as a function of stimulus current for one or more postures. The sensitivity of a patient's neural response to changes in stimulation current can be measured from the slope of the activation plot.

1.3.6 Data recording and patient compliance

While the patient is using their stimulator, various usage and measurement data are recorded on the stimulator. This data includes stimulation status (on/off), closed-loop status (enabled/disabled), ECAP amplitude, stimulation current, and patient interactions with the device. This data is downloaded via the CPA and can be viewed in the RECAP Viewer.

1.3.7 Neural response profile (NRP)

The neural response profile is a set of objective measures characterizing the spinal cord activation levels experienced by the patient while using their stimulator. Activation level (ECAP amplitude) is continuously recorded and compressed into histogram bins on the stimulator for later analysis on the RECAP Viewer.

1.3.8 Conduction velocity (CV)

ECAP recordings can be used to determine the conduction velocity of the dorsal column fibers being stimulated. ECAPs are recorded using the CPA and analyzed using the RECAP Viewer to calculate their velocity. Changes in the population of fiber sizes activated and fiber properties may be detected through changes in CV.

1.3.9 Chronaxie and rheobase (strength-duration curve)

ECAP amplitudes recorded at different stimulation pulse widths can be used to objectively calculate chronaxie and rheobase for fibers activated during spinal cord stimulation. Changes in axonal excitability or distance from electrode may be detected through changes in chronaxie or rheobase.

1.3.10 Lead offset

The vertical alignment of two implanted leads may be estimated using the lead offset check feature in the CPA. The offset between two leads may be used to guide the choice of stimulation and measurement electrodes.

1.4 System Components

1.4.1 Evoke Closed-Loop Stimulator (CLS)

Ref No. 3002, 3042

The Evoke Closed-Loop Stimulator (CLS) is a totally implanted spinal cord stimulator that connects to the CAP12 Percutaneous Leads and is implanted under the skin for long-term therapy. The CLS delivers either closed-loop or open-loop stimulation through the leads and measures the neural response to stimulation. A port plug is provided with the CLS, for insertion into an unused CLS port when only one lead is implanted.

1.4.2 Evoke External Closed-Loop Stimulator (eCLS)

Ref No. 3036

During the trial stimulation period, the CAP12 Percutaneous Leads are connected to the Evoke External Closed-Loop Stimulator (eCLS). The eCLS is an external stimulator used for intraoperative testing and during the trial stimulation period. The eCLS delivers either closed-loop or open-loop stimulation through the leads and measures the neural response to stimulation.

1.4.3 Evoke eCLS Case

Ref No. 3035

The Evoke eCLS Case is used by the patient to house the eCLS during the trial stimulation period. The kit also includes two lead adapters to connect the leads or lead extensions to the eCLS.

1.4.4 Evoke CAP12 Percutaneous Lead Kit, 60cm and 90cm

Ref No. 3008/3016/3009/3017

The Evoke CAP12 Percutaneous Leads are placed in the epidural space overlying the spinal cord and are connected to an eCLS for a trial stimulation period, or to a CLS for long-term therapy. One or two leads, each with 12 electrodes, are implanted. The lead kit is provided with one suture anchor to secure the lead, and surgical accessories (epidural needle and two stylets) for use during lead placement.

1.4.5 Evoke CAP12X Lead Extension Kit, 55cm

Ref No. 3011

The Evoke CAP12X Lead Extensions are used when trialing a permanently implanted lead, where the extension is externalized for connection to an eCLS.

1.4.6 Evoke Active Anchor Kit

Ref No. 3043

The Evoke Active Anchor allows the surgeon to secure the lead after placement in the epidural space. The active anchor kit is provided with two active anchors and a torque wrench to tighten the anchor.

1.4.7 Evoke Intraoperative Cable Kit

Ref No. 3034

The Evoke Intraoperative Cable allows the surgeon to connect the eCLS to the implanted leads for intra-operative testing.

1.4.8 Evoke Patient Controller (EPC)

Ref No. 3040

The Evoke Patient Controller (EPC) allows the patient to control their therapy and actively monitors the stimulator battery status and other elements of the system. The EPC and the stimulator communicate with each other wirelessly.

1.4.9 Evoke Charger

Ref No. 3006

The Evoke Charger allows the patient to recharge the battery in a CLS. The Charger coil (attached to the Charger) is placed over the CLS and charge is transferred to the CLS through thin clothing and the skin. The Charger kit also includes a power adapter for recharging the Charger.

1.4.10 Evoke Accessory Belt

Ref No. 3039

The Evoke Accessory Belt is an elastic belt with a pouch to hold an eCLS or Charger coil.

1.4.11 Evoke Clinical Interface (CI)

Ref No. 3024

The Evoke Clinical Interface (CI) is a tablet computer with a preinstalled programming application (the Clarity Programming Application, CPA) used by the clinician to adjust the therapy settings of the Evoke CLS and eCLS.

1.4.12 Evoke Clinical System Transceiver (CST)

Ref No. 3004

The Evoke Clinical System Transceiver (CST) is a plug-in device (USB connection) that enables exchange of information wirelessly between the CI and the stimulator.

2. Indication for use

The Saluda Medical Evoke SCS System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following:

- Failed back surgery syndrome
- Intractable low back pain and leg pain
- Diabetic peripheral neuropathy of the lower extremities

2.1 Contraindications

The Evoke SCS System should not be used in patients who:

- Do not receive effective pain relief during trial stimulation.
- Are unable to operate the Evoke SCS System.
- Are unsuitable surgical candidates.

3. Safety Information

For general system warnings and precautions refer to the Evoke SCS System Surgical Guide, accessible at https://www.saludamedical.com/manuals.

The Evoke CI is a tablet computer. For non-therapy specific warnings and precautions on this product refer to the device manual accompanying the CI tablet.

3.1 Warnings

⚠**Use in diabetic patients:**

- The physiologic closed-loop controlled (PCLC) stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.
- Frequencies greater than 1200 Hz have not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

3.2 Precautions

3.2.1 Unsupported software applications

⚠Do not load additional software applications onto the Evoke CI. The Evoke CI has all the necessary software required to interact with and program the Evoke SCS System from Saluda Medical. Other applications could interfere in unpredictable ways with the programming software installed and affect the delivery of therapy for patients. Any required software installations shall be supported directly by Saluda Medical representatives or via detailed instructions concerning specific installations as required.

3.2.2 Unsupported hardware

⚠Do not connect any device to the Evoke CI other than the supplied**:** keyboard, power adapter and Evoke CST. Do not connect the Evoke CST to any device other than a Saluda Medical supplied Evoke CI. Unsupported hardware could interfere in unpredictable ways with the programming software installed and affect the delivery of therapy for patients. Do not modify, tamper, or use other equipment with the Evoke SCS System.

For data file extraction, it is permissible to use an external USB memory stick that has passed a screening check by an up-to-date anti-virus software application, but no files should be transferred onto the CI unless otherwise instructed by Saluda Medical to do so.

Use of accessories, transducers and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation

3.2.3 Shared IT networks

⚠Network connection (via Wi-Fi) is only permitted to secure networks. Connecting to unsecure networks could lead to the modification of the CI system or software that interfere in unpredictable ways with the programming software installed and affect the delivery of therapy for patients.

3.2.4 Modification of the programming software

⚠Do not attempt to modify the Clinical Programming Application (CPA) software which comes preinstalled on the CI for the programming of Saluda Medical neurostimulators. Any deletion or modification of files associated with the CPA could adversely affect the system's ability to effectively adjust therapy for patients.

Required software upgrades will be supported directly by Saluda Medical representatives or via detailed instructions concerning specific upgrades as required. Additionally, any stimulator software upgrades will be fully supported by Saluda Medical representatives – do not attempt to modify the stimulator software without Saluda Medical's instruction.

3.2.5 Non-sterile components

⚠**DO NOT STERILIZE** the CI, CST, eCLS, EPC or Charger; these items are not to be sterilized and doing so could irrevocably damage the devices.

3.2.6 Clinical staff training

⚠Clinical staff using the CI/CST to program the Evoke SCS System must be adequately trained in the programming of SCS systems generally. Additionally, clinical staff programming the Evoke SCS System should have been trained based on the instructions within this manual. A poor understanding of the programming of SCS systems generally, and the Evoke system specifically, could cause unpleasant or painful stimuli for patients.

3.2.7 Electromagnetic interference (EMI)

⚠As the CI communicates via the CST to the neurostimulator (eCLS or CLS) wirelessly, the quality of this connection can be adversely affected by some types of electrical equipment that generate EMI. Such equipment should be avoided where possible when programming and/or suspected if communication between stimulator and CI/CST is poor. Examples of such equipment found in clinical environments include but are not limited to: Mobile phones, electro-surgery tools, electromagnets, radiofrequency identification devices and emergency vehicle/services radios. Avoid use of the CI and CST adjacent to or stacked with other equipment, because it could result in improper operation. If such use is necessary, observe the CI, CST and the other equipment to verify that they are operating normally. Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should not be used closer

than 30 cm to any part of the Evoke System, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.

3.2.8 General precautions for the CI and CST

⚠The CI is a critical piece of equipment to enable the delivery of therapy. Always handle it with care and regularly inspect the device for damage and/or impaired functioning. Never modify the CI in any way. If you have concerns about the integrity of the CI/CST, contact Saluda Medical representatives to arrange repair or replacement. The CI runs on a rechargeable battery and can be used wirelessly or while plugged in via the power adapter supplied. Care should be taken to keep the CI well charged so it can be used in clinical environments where plug sockets are not readily available. Always have a spare charged CI available in case of malfunction. Do not use the CST at the patient's home.

3.2.9 Lead Extension

The Lead Extension should only be used as part of a trial system, to connect the lead to the eCLS (via the lead adaptor). It should **not** be implanted for connection to an implanted CLS.

4. Introduction

4.1 Evoke Clinical Interface (CI)

The CI is a tablet computer. For full specifications and instructions for use of the tablet computer refer to the device manual accompanying the CI tablet. The computer is not physically modified in any way. The CI operates on the Microsoft Windows platform. The CI is supplied with the software necessary for programming Saluda Medical stimulators pre-installed, and no other software should be installed on the device.

Upon starting and logging in to the CI, the user will immediately find a program icon  . This will lead the user into the Clinical Programming Application (CPA) that enables programming of either the Evoke eCLS or CLS.

> **Note**: Login password for the CI will be provided by Saluda Medical representatives and cannot be changed. All potential CI operators should be made aware of this password.

4.2 Evoke Clinical System Transceiver (CST)

The CST is a radio telemetry device that enables communication between the CI and the stimulator (eCLS or CLS). Commands generated through the CPA loaded on the CI are sent to the stimulator and data is received back from the stimulator to display in the CPA via the CST. The CST is connected to the CI via a USB connector and receives power from the CI via this link.

5. Clinical Interface (CI) setup

This section describes how to setup the CI and connect to a stimulator.

5.1 Connecting the CI to the CST

To program and download data from the eCLS or CLS, communication must first be established. The CST connects to the CI to communicate using a radio signal transmitted to the eCLS or CLS.

1. Turn on the CI and login to the 'Saluda' account.
2. Check that the time and date on the CI are correct (bottom right corner of CI screen). Refer to CI instructions to change the time and date.
3. Connect the CST to the CI with the USB connection.

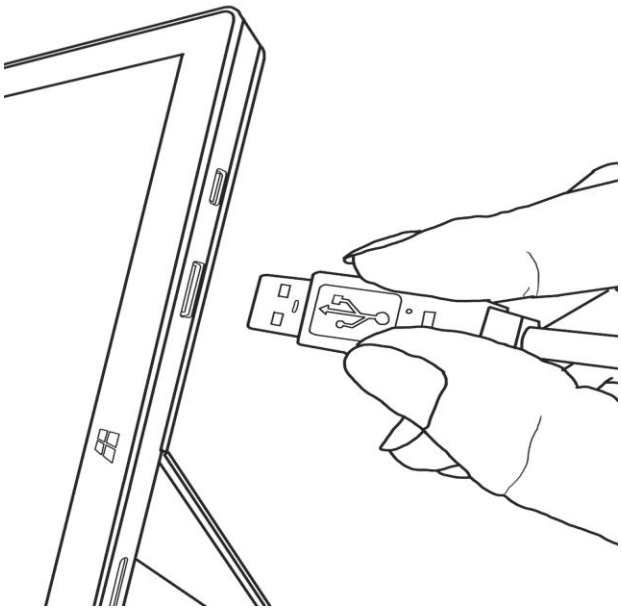


Figure 5.1: Connecting the CST to the CI USB port.

4. Position the CST near the stimulator.

   Note: The CST can link with the stimulator within a 1.0 m (3.3 ft) radius.

   Note: Electromagnetic interference can affect the quality of this wireless link; see Section 3.2.7 - Electromagnetic interference (EMI).

5.2 Starting the CPA and connecting the CI to eCLS/CLS

1. Touch the Evoke Clarity Clinical Programing Application (CPA) icon on the CI start menu (or double-tap the icon on the desktop) to start the CPA.

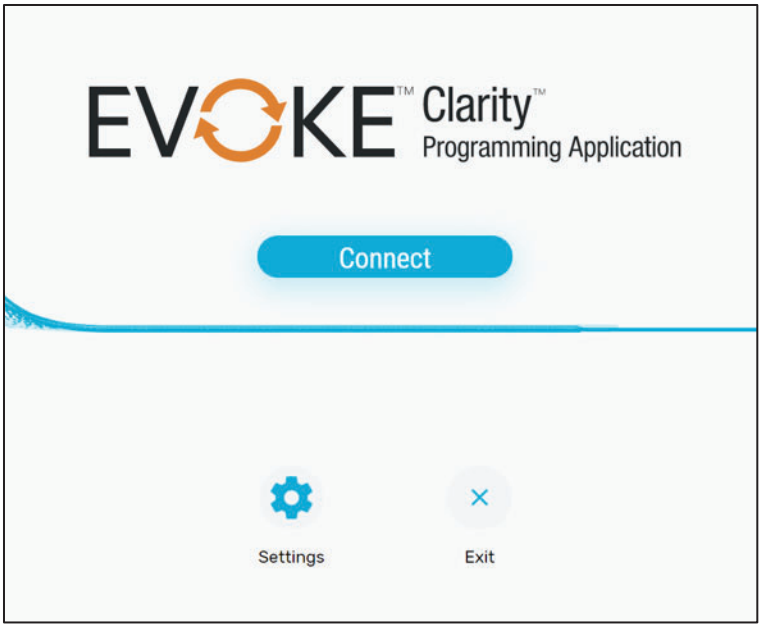


Figure 5.2: Start Screen.

2. Touch *Connect* on the start screen to access the Connect screen (as shown above). A scan for nearby stimulators will begin automatically, and a list of stimulators within range will appear on this screen (example shown in Figure 5.3).

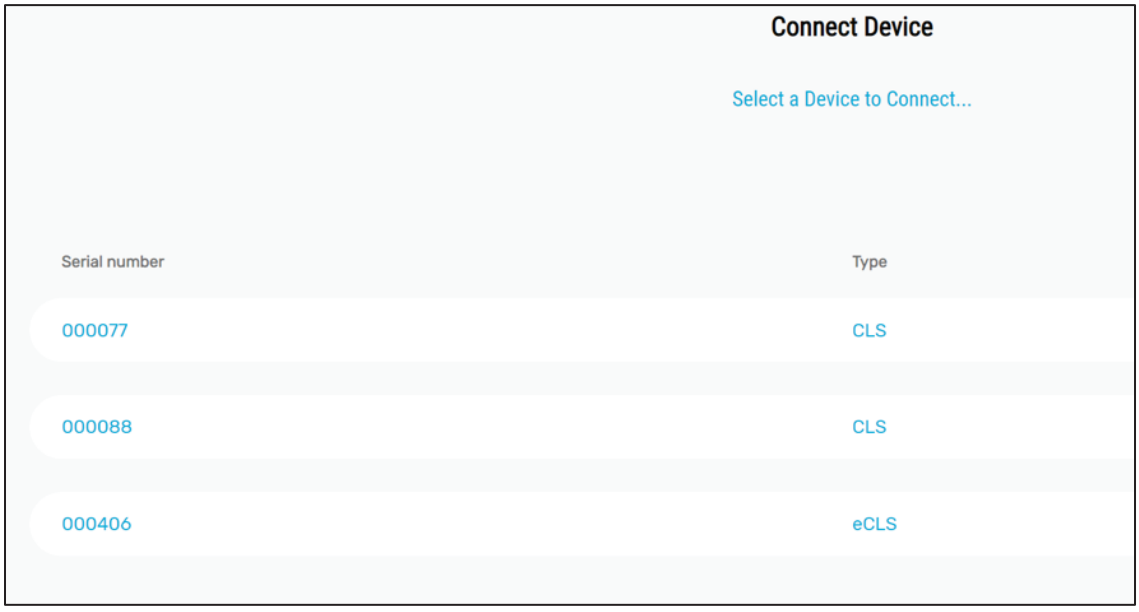


Figure 5.3: Connect screen showing the result of a scan for nearby stimulators.

3. Select the device you wish to connect to, based on serial number and type (see Figure 5.3).

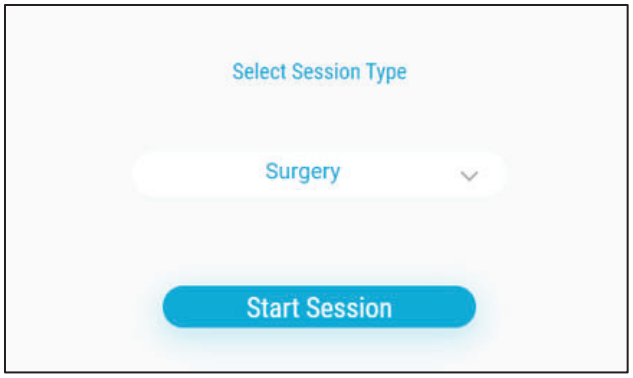


Figure 5.4: Select Session Type.

4. The CPA will connect to the stimulator and retrieve some stimulator data (such as patient ID, battery level, and programs).

   ⚠ **Caution**: Before connecting the CPA to the stimulator, ensure that you have a magnet and paired EPC available at all times during the programming session in case they are needed to stop stimulation (refer to the Evoke SCS System User Manual).

5. Select Session Type from the dropdown menu and touch the Start Session button to start your programming session (see Figure 5.4). The programming session will begin on the home page (see Section 6.2).

6. Using the Clarity Programming Application (CPA)

This section describes the layout of the Clarity Programming Application (CPA) and how to use it to setup a new patient profile and complete a programming session.

6.1 CPA Main Screen Layout

The components of the CPA Main screen are displayed throughout the programing session and are shown below in Figure 6.1.

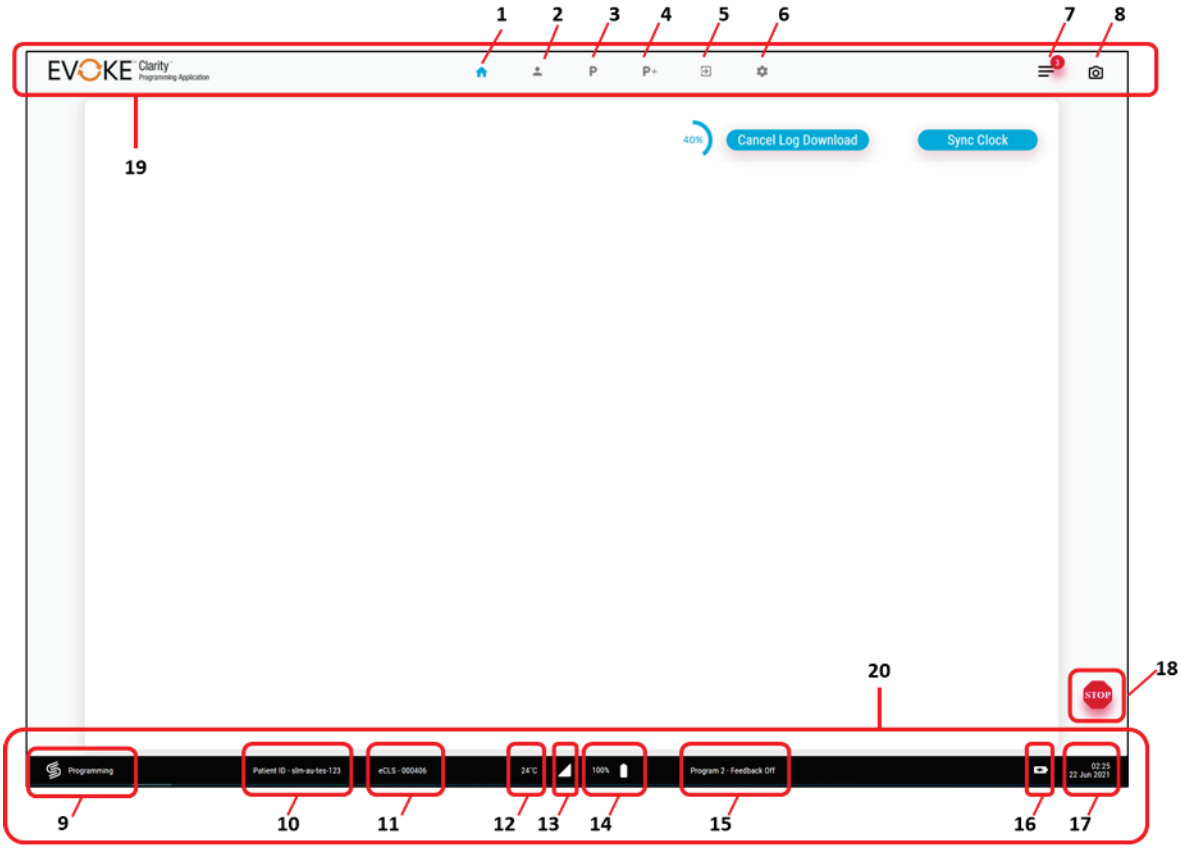


Figure 6.1: Static outer CPA screen layout.

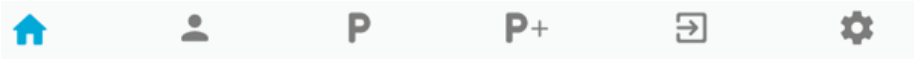
1. Home page
2. Patient page
3. Programming page
4. Neurophysiological Measurements page
5. Disconnect page
6. Settings page
7. Notes pop-up
8. Screenshot button
9. Session type
10. Patient ID
11. Stimulator Serial Number
12. Stimulator Temperature
13. Telemetry Strength
14. Stimulator Battery
15. Program Number and Feedback Status
16. CI Battery
17. CI Time and Date
18. Stop Therapy
19. Header
20. Status Bar

6.1.1 Header and Status Bars

The header and status bars will be present at all times after you have connected to a device and started a session. Likewise for the *Stop* button.

The header bar contains:

1. The menu bar for accessing different pages,



2. Notes button (for bringing up the Notes pop-up window).



Note: There is an area to the left of the Notes button where you may see a black banner with a message that appears for 5 seconds; see Section 6.1.2 for additional information about notifications.



3. A button for taking screenshots.



The status bar (footer) contains:

1. Information about the session, i.e. session type (on the left)



2. Information about the connected device, such as patient ID, serial number, temperature, communication quality indicator, battery level, and current program.



3. Information about the CI (on the right), such as battery level, time, and date.



6.1.2 Display of Notifications

Events and alerts are displayed in the CPA using various notification types depending on the immediate significance to the user (described in more detail in the following pages). The different notification types, in order of importance, are:

1. **Pop-up:** Alerts that require immediate attention and possible action from the user or events regarding important functions that completing successfully.
2. **Banner:** Common events and alerts (this is the most frequent form of notification).

3. **Button icon:** Alerts regarding an issue with a specific feature/button.

In some cases, alerts may result in multiple notification types (See example in Figure 6.2).

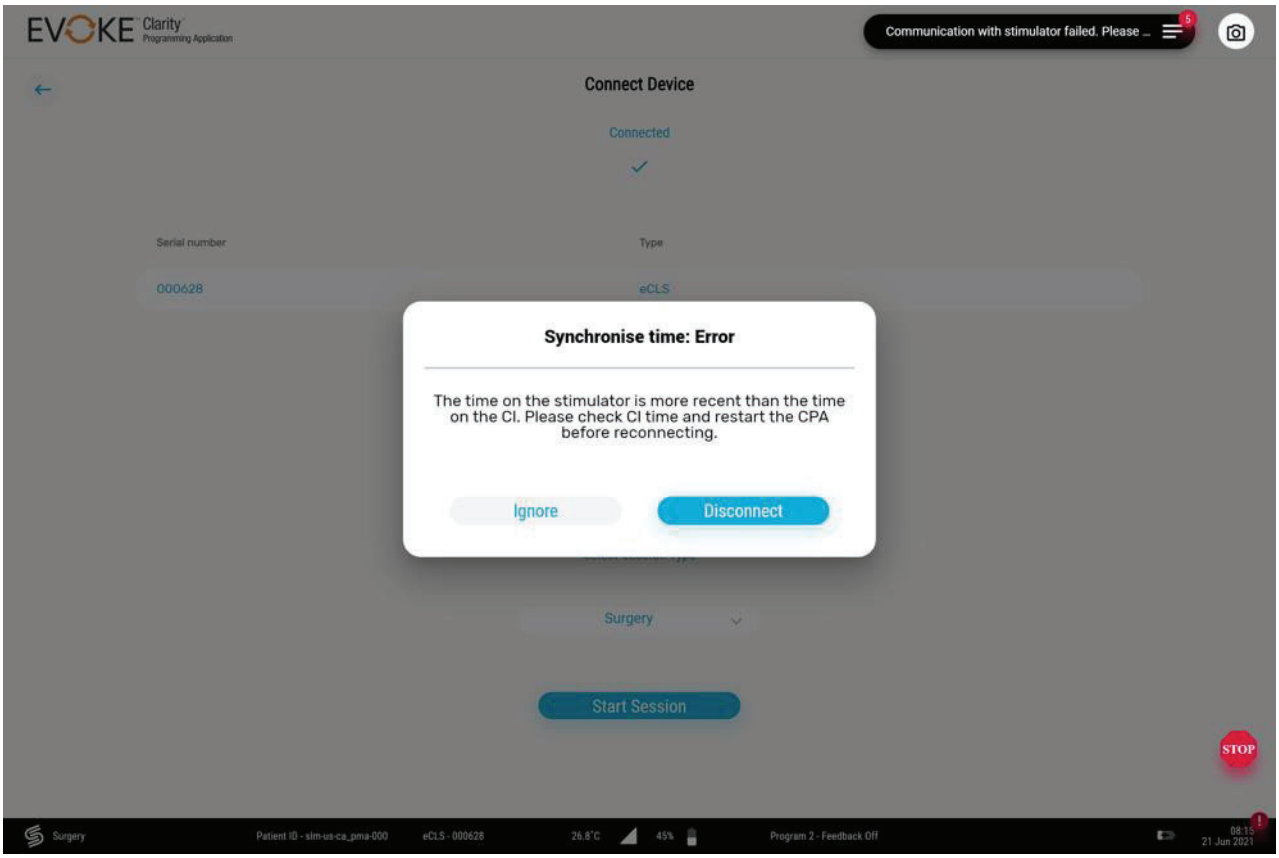


Figure 6.2: Example of an alert generating both a banner and a pop-up.

Alerts and events are also viewable in the *Notes* window (see Section 6.2.4). When either of these occur, the number above the *Notes* icon will be incremented to let the user know there is new information 

. Clicking on the *Notes* button will scroll to the most recent note and reset the counter (Figure 6.3).

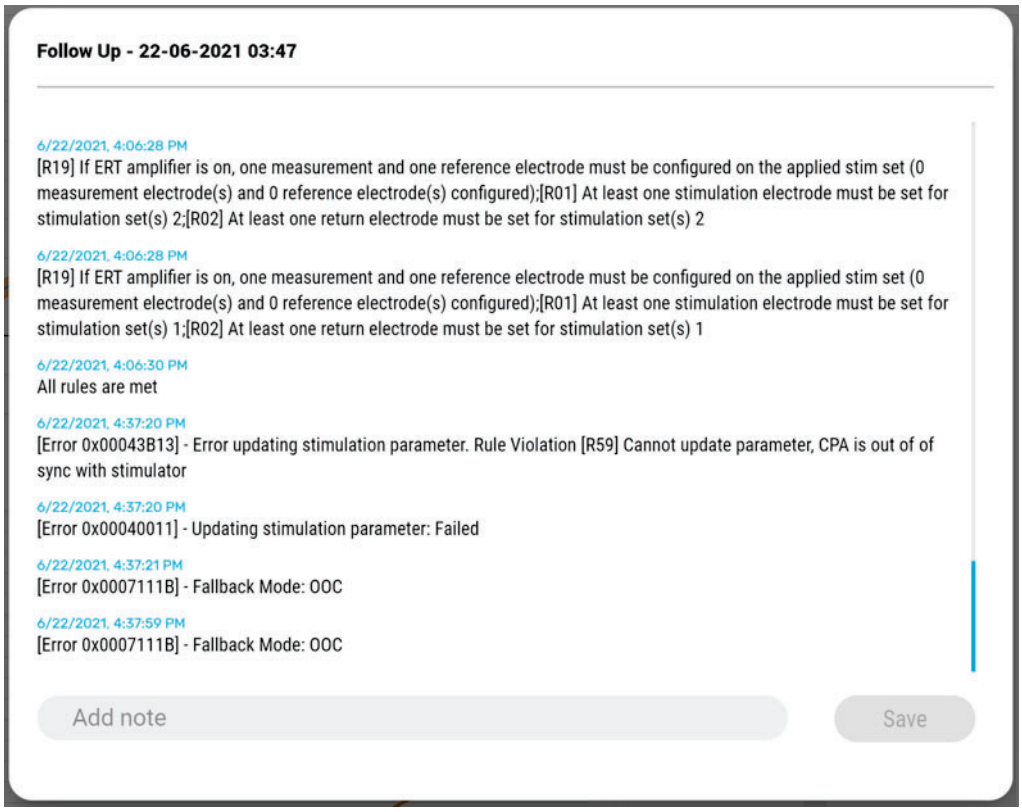


Figure 6.3: Multiple events and alerts displayed in the *Notes* window.

For more information regarding how the stimulator responds to certain alerts see Section 8.

6.1.2.1 ***Pop-ups***

Pop-up alerts notify the user of an event that requires immediate attention. They may require an action from the user or simply an acknowledgement before proceeding further (Figure 6.4).

Note: The *Stop* button is always available, even when a pop-up is obscuring the screen.

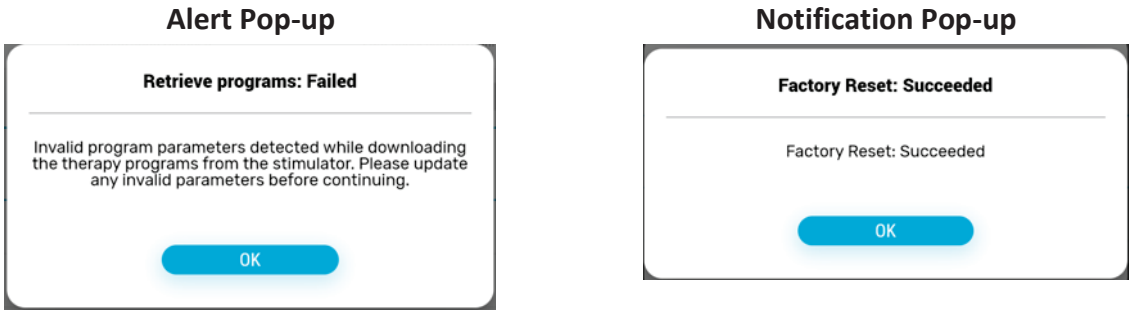


Figure 6.4: Example of pop-up alerts and notifications.

6.1.2.2 *Banners*

Banners are the most common form of notification, letting the user know a certain alert has been triggered. In some cases, they also indicate what needs to be done, or that a task has completed successfully (Figure 6.5).



Figure 6.5: Example of banner alerts and notifications.

6.1.2.3 *Button icons*

Certain alerts will trigger an *alert* icon to appear over a button to let the user know there is an issue with or relating to that feature. Clicking on the *alert* icon will result in additional information being displayed about the issue(s). See example in Figure 6.6.

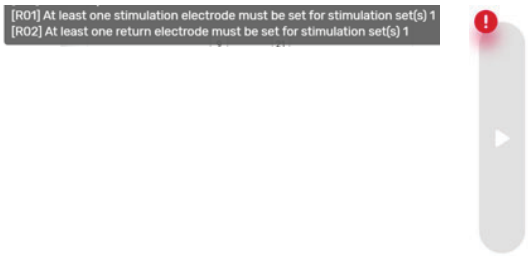


Figure 6.6: Example of an *alert* icon over a button and the information displayed when the icon is clicked.

If a parameter has been updated in the CPA, but not yet sent to the stimulator, a 'sync' icon will appear over the unsync'd parameter and the associated program number to let the user know the CPA and stimulator are not synchronized (Figure 6.7).

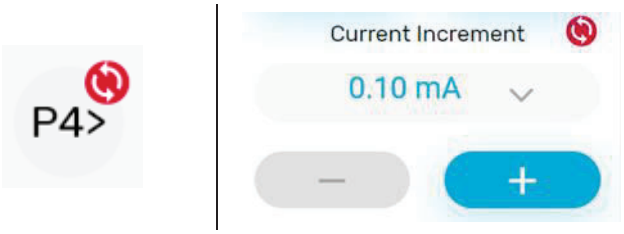


Figure 6.7: *Left:* One or more parameters of a program has not been sent to the stimulator. *Right:* The current increment for the selected program has not been sent to the stimulator.

6.1.2.4 *Safe Mode errors*

A Safe Mode error will be indicated with an initial pop-up and a persistent banner notification that will remain until the issue has been resolved (Figure 6.8). Safe Mode errors must be cleared

before stimulation can continue. A Safe Mode error is also indicated with the *Contact Clinician* indicator on the patient's EPC and Charger (see Evoke SCS System User Manual).

If a Safe Mode error is encountered:

1. Save the programs on the stimulator (if you want to keep them and they have not already been saved).
2. Perform a 'Soft Reset' using the CPA to take the stimulator out of Safe Mode (see Section 6.7 for where to find the *Soft Reset* button).

   Note: The pop-up that is trigged by a Safe Mode error enables the user to perform a 'Soft Reset' without going to the *Settings* screen.
3. Report the occurrence of the Safe Mode error and accompanying code to Saluda Medical.

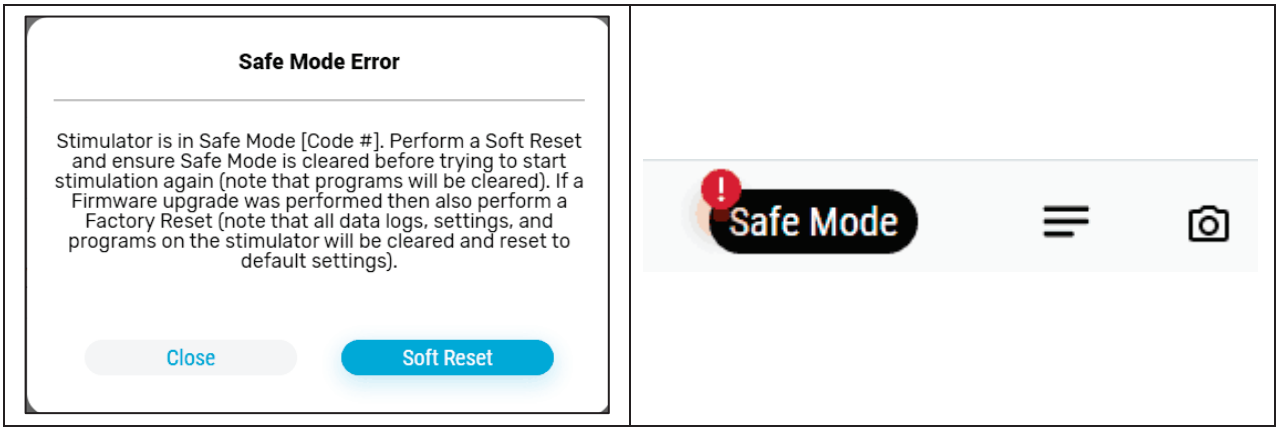


Figure 6.8: *Left*: Pop-up indication that the stimulator is in *Safe Mode* ('#' will be the error number) and the subsequent steps required. *Right:* The persistent banner notification will be displayed until the stimulator is no longer in *Safe Mode*.

6.1.2.5 *Communication Quality Indicator*

The quality of the radio communication between the CST and the stimulator is indicated on the status bar, see examples in Figure 6.9.

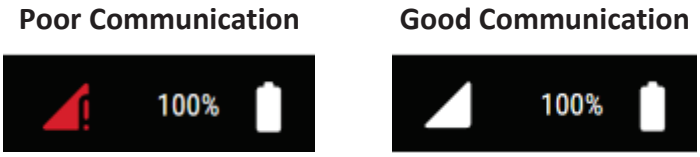
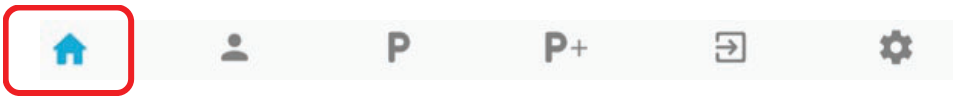


Figure 6.9: States of the communication quality indicator, shown adjacent to the stimulator battery level.

If there are any notifications regarding poor communication (e.g., a banner or the communication quality indicator), do not make any further changes to the program until communication is restored. If there are frequent failed commands and/or extended time between the response to commands, move the CST closer to the stimulator to improve communication. If issues persist,

stop stimulation (see Section 6.4.4.1) until communication with the stimulator is re-established. If unresolved, restart the CPA or the CI.



6.2 Home Page

The home page is the first page you see after connecting to a device and starting a session. This is where logs are downloaded from the stimulator, and the clock of the stimulator is synchronized with the CI clock.

6.2.1 Download logs

If stimulation is off, then logs will automatically download upon entry to this page. You will see a progress indicator showing how much time remains to complete the download.

Note: Depending on the amount of data saved on the device this could take several minutes. Downloading can be cancelled but this is not recommended as any system error and device usage logs will be missed.

If logs don't download automatically, then touch the STOP button to stop stimulation, and then touch the Download Logs button.

The CPA will display *Logs Successfully downloaded* in the header when it has successfully connected and downloaded all of the logs from the stimulator (see Figure 6.10 for an example of this banner notification).

Note: If any logs cannot be downloaded, an error message will be displayed in the Notes.

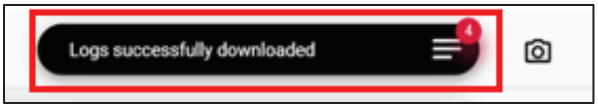


Figure 6.10: Logs Successfully downloaded.

Log is maintained when the system is powered down and contents are unaffected after the device has experienced a total loss of power.

6.2.2 Set stimulator time

The stimulator time is normally synchronized automatically to the CI time during connection and data download (except when stimulation is on during connection).

1. Check that the time and date on the CI are correct (bottom right corner of CPA screen, Figure 6.1) Refer to the CI instructions (see Section 5) to change the time and date, and reconnect to the stimulator after correcting the date/time on the CI.
2. Touch the *Sync Clock* Button to set the stimulator time to the CI time (if the time is not

already synchronized).

6.2.3 Check stimulator battery status

The stimulator battery status is displayed in the status bar (see examples in Figure 6.11 and Figure 6.12). If the battery voltage is low (≤28% full) the battery icon will be red. Refer to the Evoke SCS System User Manual for instructions on charging the CLS battery or to the Evoke SCS System Surgical Guide for charging the eCLS battery.



Figure 6.11: Stimulator battery status**.**



Figure 6.12: Stimulator battery status – battery is low voltage.

6.2.4 Notes

During a programming session the data may be annotated with a time-stamped note.

A number will appear next to the Notes button to indicate how many notes, notifications, or alerts have been added since the last time you opened the Notes pop-up window 

.

1. Open the Notes pop-up window.
2. Type a text note in the *Add note* field.
3. Touch the *Save* button to save the text note with a time-stamp in the clinical data log file.
4. A screenshot of the CPA programming screen is also saved in a 'Screenshot' folder for this visit, and can be easily retrieved from within the Notes pop-up window.

6.2.4.1 *Other system generated notes*

In addition to manually entered notes, the system also records a note (and saves a screenshot) in the following situations:

1. When the activation plot level markers (T, C-, C+, M) are activated (from the P page)
2. When Start AP and Stop AP buttons are touched on the F tab (from the P page).
3. When a posture is selected and deselected in the E tab (from the P page).
4. When Neurophysiological Measurement workflows start and end (from the P+ page).

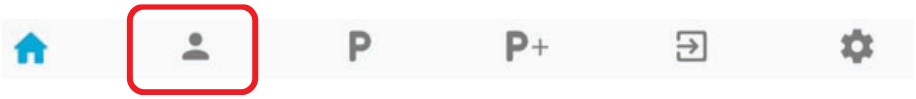
6.2.5 Screenshots

In addition to the automatically generated notes and screenshots mentioned above, screenshots may be saved manually.

1. Touch the screenshot button  to save a screenshot of the CPA programming screen.
2. A number next to the Notes button will increment to reflect the addition of this note to

the list of screenshots  .

3. The screenshot is saved in a ‘Screenshot’ folder for this visit and can be easily retrieved from within the Notes pop-up window.



6.3 Patient Page

Within the Patient page there are two main tabs:

1. Patient Profile Tab  .
2. Patient Survey Tab  .

The Patient Profile should be completed before the stimulator is programmed for the first time. Patient Surveys may be available to document more information about the session, patient demographics, and pain history. They are also used to generate the RECAP Visit report.

6.3.1 Patient Profile for a new patient

1. Touch the Patient Profile Tab  .
2. Check the appropriate ‘Consent’ setting (yes/no) provided by the patient.
3. Complete the profile information to automatically generate a Patient ID.
4. Complete the Patient ID by adding the patient’s 3-digit number to the end of the ID. This will also be displayed in the status bar.



Figure 6.13: Example of a completed Patient ID.

6.3.2 Retrieve Patient Profile for an existing patient

1. Patient Profile information is retrieved from the stimulator on connection and displayed on the *Patient Profile* page (see Figure 6.13).
2. Ensure the correct 'Consent' setting is selected and adjust if it has changed since the previous visit.
3. Check that all fields in the Patient Profile have been retrieved and are correct.

6.3.3 Patient Survey

A survey may be completed to document the patient's demographics, pain history, and experience with SCS.

1. Touch the Patient Survey Tab .
2. The Surveys list displays all the surveys that have been created on the device (see example in Figure 6.14). The first survey created will always be the 'Baseline' survey. Any subsequent surveys will be 'Follow Up'.

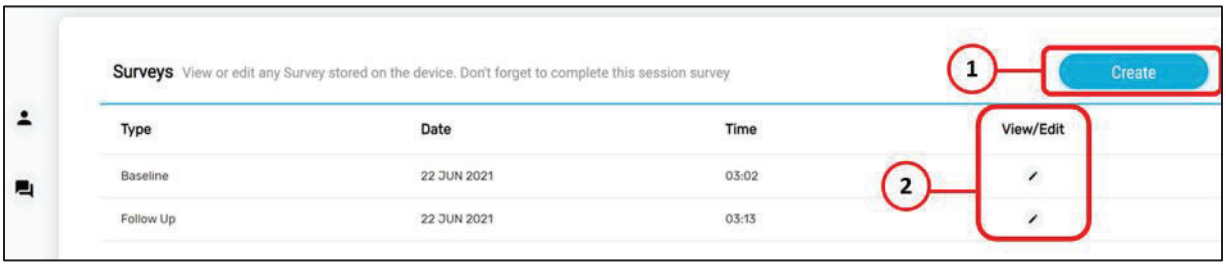


Figure 6.14: Survey list.

1. Create a new survey
2. View/Edit survey

3. If more than 2 surveys have been created and saved to the device, the CPA will only automatically download the baseline survey and most recent follow-up survey.

6.3.3.1 *Baseline Patient Survey Data*

The Baseline Patient Survey is used to document information about the patient and their pain, prior to SCS. This survey information will be used to populate the follow-up surveys in order to compare how the patient is doing throughout their experience with SCS.

1. Touch Create
2. A new baseline survey will open

Within the survey, there are five pages, as shown in Figure 6.15.

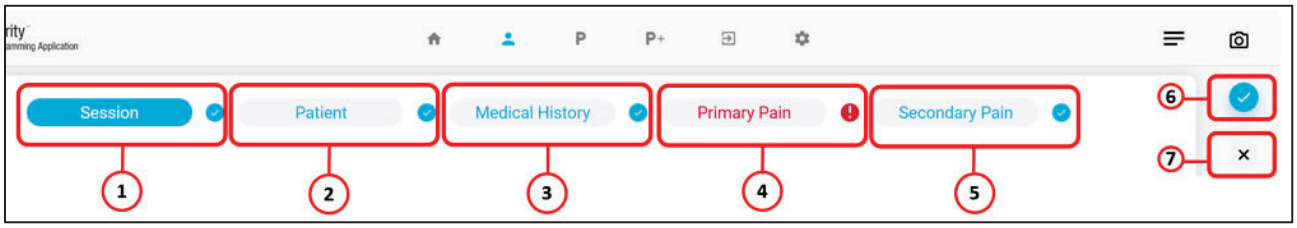


Figure 6.15: Survey Page Layout.

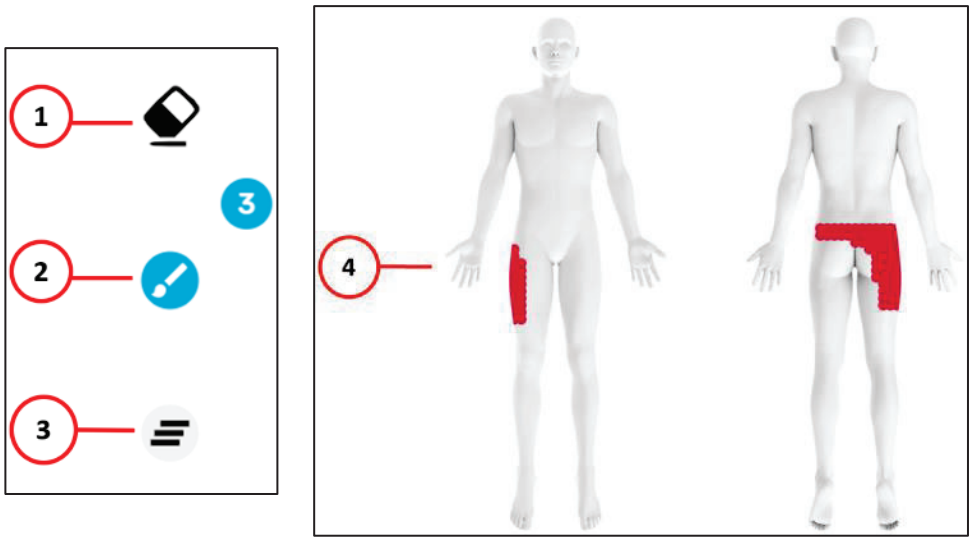
1. Session page
2. Patient page
3. Medical History page
4. Primary Pain page
5. Secondary Pain page
6. Save Survey button
7. Close Survey button

The colored page header (i.e. 'Session' in the above example) is the survey page currently being displayed. If there is a checkmark next to the page header, the page is either fully completed or complete enough to be saved. If there is a alert icon next to the page header (and the font is red), the page is incomplete and needs to be filled out before saving the survey. Information listed in the table below in **bold** are only available in Baseline surveys.

Table 6.1: Baseline Survey Information Collected.

Page Name	Key information collected
Session	Visit Reason, Physician Information, Patient Goals
Patient	Demographics and CLS Activation Date
Medical History	**Previous Neuromodulation Treatments** and Medications
Primary Pain	**History of pain**, Pain Drawing and Scores, QOL
Secondary Pain	Pain Drawing and Scores

6.3.3.2 *Shading Body Areas*



1. Eraser Tool
2. Paint Brush Tool
3. Clear All Tool

Figure 6.16: Legend for shading body areas.

1. The Eraser and Paintbrush Tool have 3 resolutions options: 1, 2, 3. Both default to 3, to be used for broader strokes, while 1 is to be used for finer strokes.
2. If you want to clear the entire drawing, select the 'Clear All' button. A pop up will confirm if you want to clear shading.

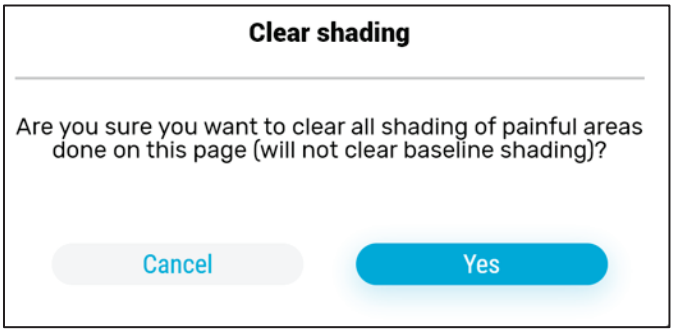


Figure 6.17: Clear shading.

6.3.3.3 *Save the Survey*

Touch the ✓ to save the Survey to the stimulator (Figure 6.15).

6.3.3.4 *Close the Survey*

If you need to exit the survey prior to completing and saving, there are two options.

1. Option 1: Touch the ×. This will bring up a pop-up message confirming that you want to close the survey without saving.

- Touch 'Yes' to confirm.

2. Option 2: Touch any of the component tabs at the top of the screen (i.e. P). This will bring you to the selected page (i.e. the program page).

- When you return to the Survey screen, instead of saying 'Create' at the top of the screen, it will now say 'Resume'.



Figure 6.18: Survey Screen after closing a survey without saving.

- To continue editing the survey, touch 'Resume'. A Resume Survey pop-up window will appear, asking if you want to resume or create a new survey. Touch 'Resume' to continue editing the survey. Touch 'New Survey' to discard the survey you exited.

6.3.3.5 *Follow-up Patient Survey*

Data is pulled into the Follow-up Survey either from the baseline survey or the latest Follow-up survey, whichever is more recent. Information listed in the table below in **bold** are only available in Follow-up surveys. Some of this data is used in the RECAP Visit Report-Session Outcomes.

Table 6.2: Follow-Up Survey Information Collected.

Page Description	Key information collected
Session	Visit Reason, Physician information, Patient Goals, **Preferred Program**
Patient	Demographics, CLS Activation Date, **Satisfaction**
Medical History	Previous Neuromodulation Treatments and Medications
Pain	Pain Drawing and Scores & QOL
Sensation	Stimulation Sensation Information



6.4 Programming Page

The Programming page is where you set and adjust stimulation for the stimulator. Within the Programming page there are several tabs on the left-hand side that go through a typical programming session workflow. Along the bottom of the Programming page, there are several Thumbnails that can be selected to personalize and configure which Displays you'd like to see on the screen at any given time.



Figure 6.19: Programming Page Layout.

1. Impedance tab
2. Lead Orientation tab
3. Coverage tab
4. Acquisition tab
5. Filter tab
6. Evaluation tab
7. Program Settings tab
8. Electrode display thumbnail
9. ECAP display thumbnail
10. Activation Plot display thumbnail
11. Rolling Plot display thumbnail
12. Current (mA) display thumbnail
13. ECAP amplitude (µV) display thumbnail
14. Right control panel

For every programming session:

1. Use the Impedance tab to measure the electrode impedances to determine if all connections are intact (see section 6.4.1).
2. Use the Lead Orientation tab to set up or confirm lead orientation (which lead is on which

side, and relative offset) (see section 6.4.2).

3. Follow the Coverage, Acquisition, Filter, and Evaluation tabs (CAFE) to complete a programming session
4. Add/remove displays from the main part of the screen, at any time, using the corresponding thumbnails.

A typical programming session consists of the following steps. Refer to the subsequent sub-sections for more information on the pages and tabs used for each step.

Coverage (see Section 6.4.4)

1. Test stimulation on several electrodes and ask the patient to report where they feel paresthesia.
2. Determine the stimulation electrodes and parameters that give the best paresthesia coverage of the patient's painful dermatomal area(s).

Acquisition of ECAP (see Section 6.4.5)

3. Determine the settings that provide a good measurement of the neural response (ECAP) to stimulation.

Fitting the Filter (see Section 6.4.6)

4. Determine the filter and sensitivity settings for optimum closed-loop stimulation.

Evaluation of Settings (see Section 6.4.7)

5. Assess the performance of closed-loop stimulation with different postures.
6. Review and adjust the final program settings for the program (see Section 6.4.8).
7. Save the program to the eCLS/CLS memory and proceed to set up a maximum of four programs.

6.4.1 Impedance Tab

Measure the electrode impedances to determine if all connections are intact between leads, any lead adapters, and the stimulator.

1. Touch **P** in the header to get to the Programming page.
2. Touch the Impedance Ω tab, and the Check Impedance button (see Figure 6.20).
3. The impedances on the 24 electrodes and CLS case (E25) will be shown in the electrode display (see example in Figure 6.20).
4. Optional: To keep impedances displayed on every tab, touch the **Always show impedances** toggle to enable.

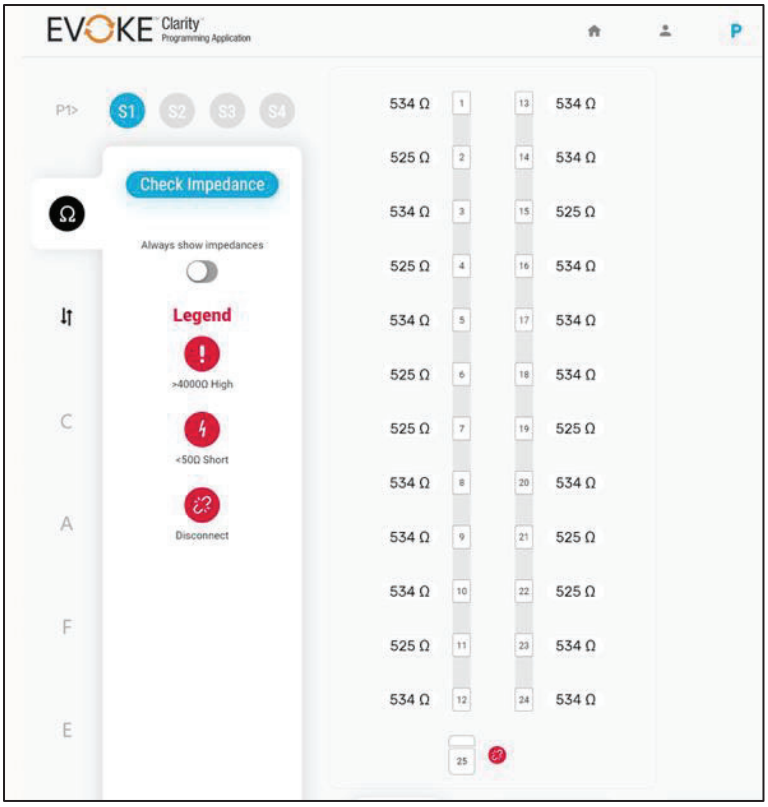


Figure 6.20: Impedances displayed on the 24 electrodes and CLS case (E25).

5. An electrode with an exclamation mark has high impedance (> 4000 Ω) and might be disconnected. A disconnected electrode shows and cannot be used for stimulation. Measurement electrodes that are disconnected will not record valid ECAPs.

   Note: The CLS case cannot be used for stimulation and may show as high impedance (> 4000 Ω). The CLS case may be used for recording even if high impedance is shown.

6. Electrodes with a lightning bolt may be shorted (< 50 Ω) and care should be taken when programming.

   ⚠ **Caution:** If the electrodes show as disconnected:

   - Wipe any blood or fluid off the lead connection contacts.
   - If the system is fully implanted, a high impedance may indicate that the lead is broken or dislodged from the header and the patient may require revision surgery if stimulation cannot be adequately reprogrammed.

   Note: When connected to an eCLS the CLS case is disconnected and cannot be used.

6.4.2 Lead Orientation Tab

1. Touch the **Lead Orientation** tab (see Figure 6.21).

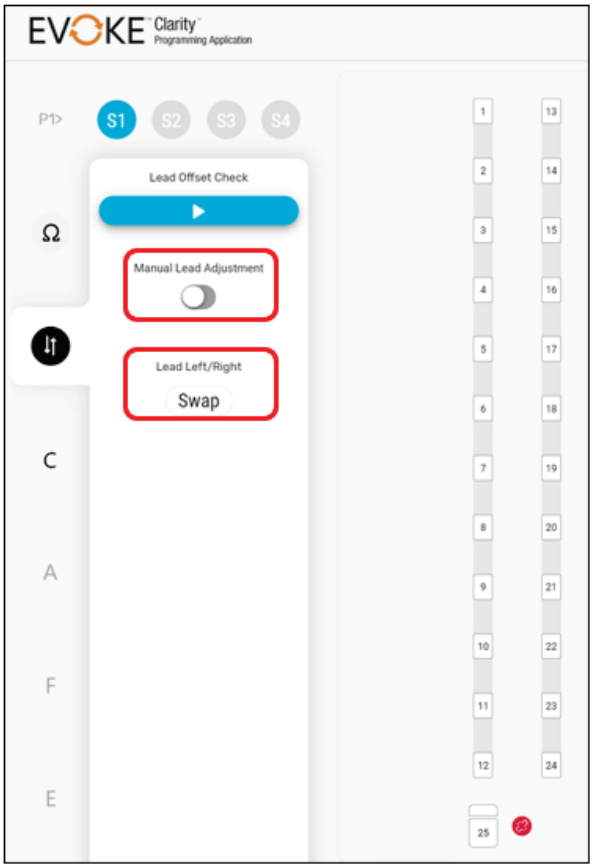


Figure 6.21: Set up Lead Orientation.

2. Touch the **Manual Lead Adjustment** toggle to enable your ability to move a lead on the screen.
3. Select and drag either lead to move it up or down.
4. Select the **Lead Left/Right Swap** button to switch sides to a position that reflects the lead location. This will aid in determining the best stimulation and measurement electrode combination.
5. **Optional:** Run the **Lead Offset Check** to estimate the vertical alignment of the implanted leads (see Section 6.4.2.1).

   Note: You can touch and drag the leads up/down on any tab to adjust the view. The orientation will remain fixed.

6.4.2.1 *Lead offset check*

Collect data to estimate the vertical alignment of the implanted leads. The lead offset check will report the peak artefact measured at different electrode locations.

To estimate the lead offset:

1. Touch the **Lead Orientation** tab .
2. Touch *Start* to start the artefact measurement.

Note: During the test, stimulation will be turned on at 0.5 mA with 200 µs pulse width, which is typically not felt by the patient.

If necessary, touch the *Stop* button STOP to stop the stimulation at any time and cancel the lead offset check.

3. Wait for the measurements to complete. The test will cycle through up to 6 stimulation locations, until sufficient data is collected.

   Note: You may stop the lead offset check at anytime by touching the *Cancel* button . The results for stimulation locations with completed measurements will be plotted, but the measurements may be invalid.

4. After completion, the results of all peak artefact measurements will be plotted (Figure 6.22).

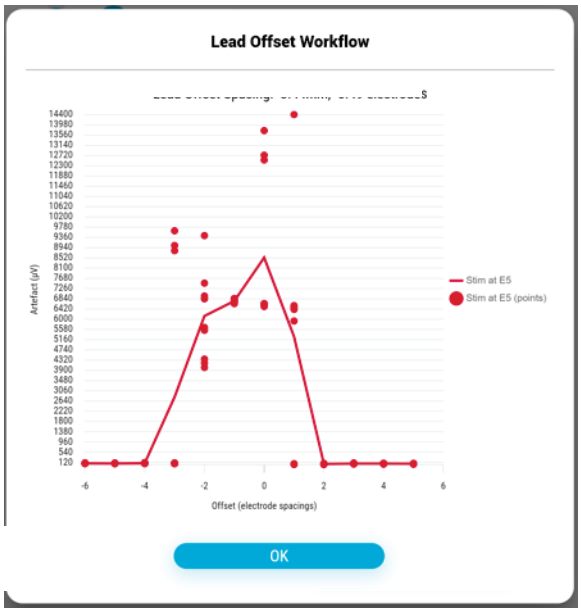


Figure 6.22 Artefact plot. The peak of the plot indicates the lead offset (electrode spacings).

Note: Negative lead offset values indicate that lead 1 (E1-E12) lies proximal to lead 2 (E13-E24). Positive values indicate that lead 1 lies distal to lead 2.

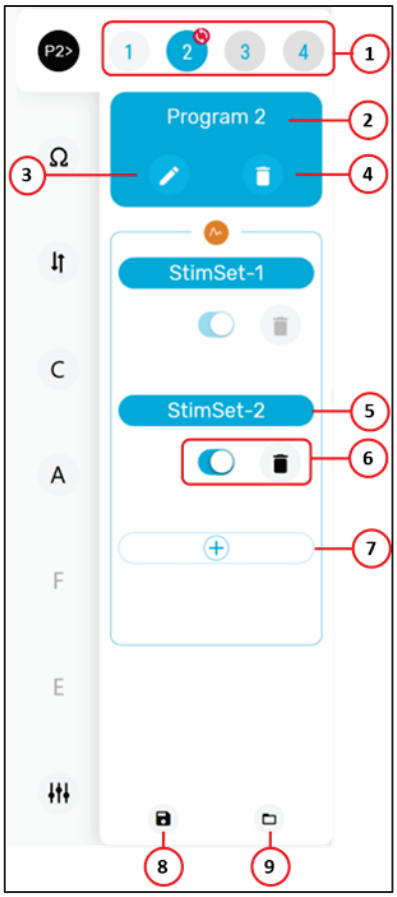
5. Click 'Ok' to close the pop-up. The original program and Stim-Set(s) parameters will be restored.

   Note: The original program still needs to be sent to the stimulator after it has been restored.

6. Refer to Section 6.4.2 if you want to adjust the lead orientation.

6.4.3 Program management Tab

The program management tab is where you change, add, delete, save, or load a Program or Stim-Set. It appears at the top of the left panel, but is normally accessed while you're in the C, A, F, or E tab. The stimulator can hold up to four different programs, each with up to four Stim-Sets (see section 6.4.4.2 for information on using Stim-Sets). Each program on the CPA is represented by a number in the Program Management tab. Any program that is run on the stimulator (with stimulation turned on) is automatically saved to the stimulator. When a program displayed on the CPA differs from what's on the stimulator, a sync icon will appear next to that number.

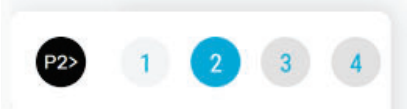


1. Program Select buttons
2. Program Label
3. Edit button (for Paresthesia Map)
4. Delete Program button
5. Stim-Set Label
6. Stim-Set Toggle and Delete buttons
7. Add Stim-Set button
8. Save Programs button
9. Load Programs from File button

Figure 6.23 Program Management tab layout.

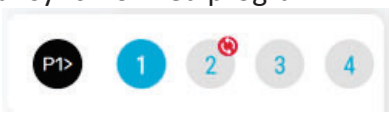
6.4.3.1 ***Select the Program to view/run/configure:***

1. Turn stimulation off before making any program configuration changes.
2. Touch the Program Number on the left panel (e.g. P1>). This will bring up the Program Management tab.

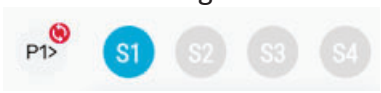


- White font on a colored (blue or orange) background represents the currently selected Program (e.g. P2 in the example above).

- Colored font on a grey background represents a Program that's not currently selected (e.g. P1 in the example above).
- Dark grey background represents a Program that is empty (e.g. P3 and P4 in the example above) and has not been enabled.
- An enabled program may still be empty if it has been selected but not configured.
- If color is blue, this means that the currently selected program has closed-loop disabled. If color is orange, this means that the currently selected program has closed-loop enabled. This color will be reflected throughout the screen elements.
- If any program on the CPA has not been run on the stimulator (such as a new program, or one that has been modified), a red sync icon will appear next to the number of the unsynchronized program.



- If you navigate away from the Program Management tab, a red sync icon will appear next to the Program Number (e.g. P1>).



- Once a program has been run, it will be saved to the stimulator and the sync icons will go away.

3. Touch the number of the program to run/view/configure.

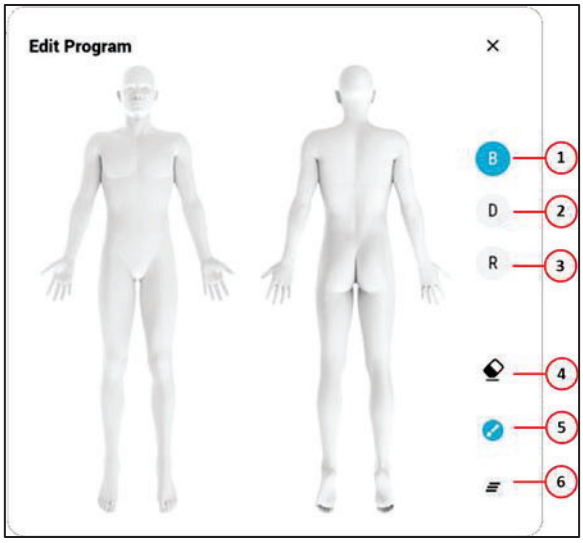
6.4.3.2 *Delete/clear a Program:*

1. Touch the number of the program you want to delete/clear.
2. Touch the trash icon  under the Program label.

6.4.3.3 *Record paresthesia information for a Program:*

1. Touch the edit icon  under the Program label.
2. A window with a body map will pop-up (see Figure 6.24).

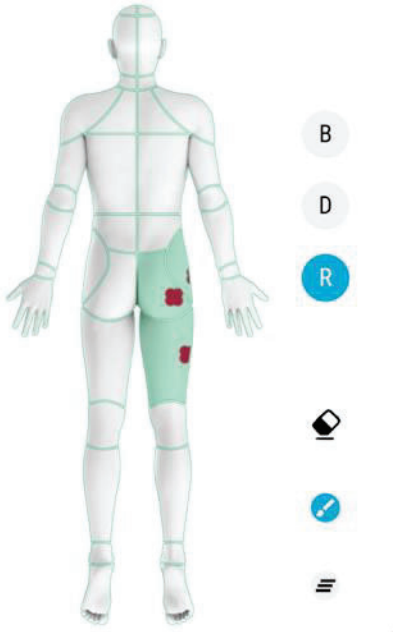
   Note: The shading information will also be saved within the SaveFile, if you save a program.



1. Blank body map view
2. Dermatome map view
3. Anatomical Regions map view
4. Eraser tool
5. Paint brush tool
6. Erase all button

Figure 6.24: Body Map window.

3. Select **B** to display a blank body map (Figure 6.24).
4. Use the touchscreen or touch pad to draw on the body map to mark the areas of paresthesia coverage associated with the selected program.
5. Touch the Eraser Tool to change your cursor from a paint brush to an eraser, if needed.
6. Touch the 'Erase all' button to erase all marks made on the current view, if needed.
7. Select **D** to change the display to dermatome map view. Entire dermatomes will be highlighted for any that contain marks made on the body map.
8. Select **R** to change the display to anatomical regions view. Entire regions will be highlighted for any that contain marks made on the body map (see example to the right).
9. Markups made in these body maps will be saved with the associated program on the CPA.



6.4.3.4 *Save Programs*

Programs are saved in two places:

1. … Into a SaveSlot in the CPA.

   There are 5 available SaveSlots. Upon connection to a stimulator, programs are loaded from the stimulator and automatically saved into SaveSlot #1 (the top-most row). A SaveSlot holds information from all 4 programs, as displayed on the CPA at the time they were saved. You can also save programs manually at any time during a programming visit.

They will go into the next available (blank) SaveSlot. If there are no blank SaveSlots, they will overwrite the oldest SaveSlot.

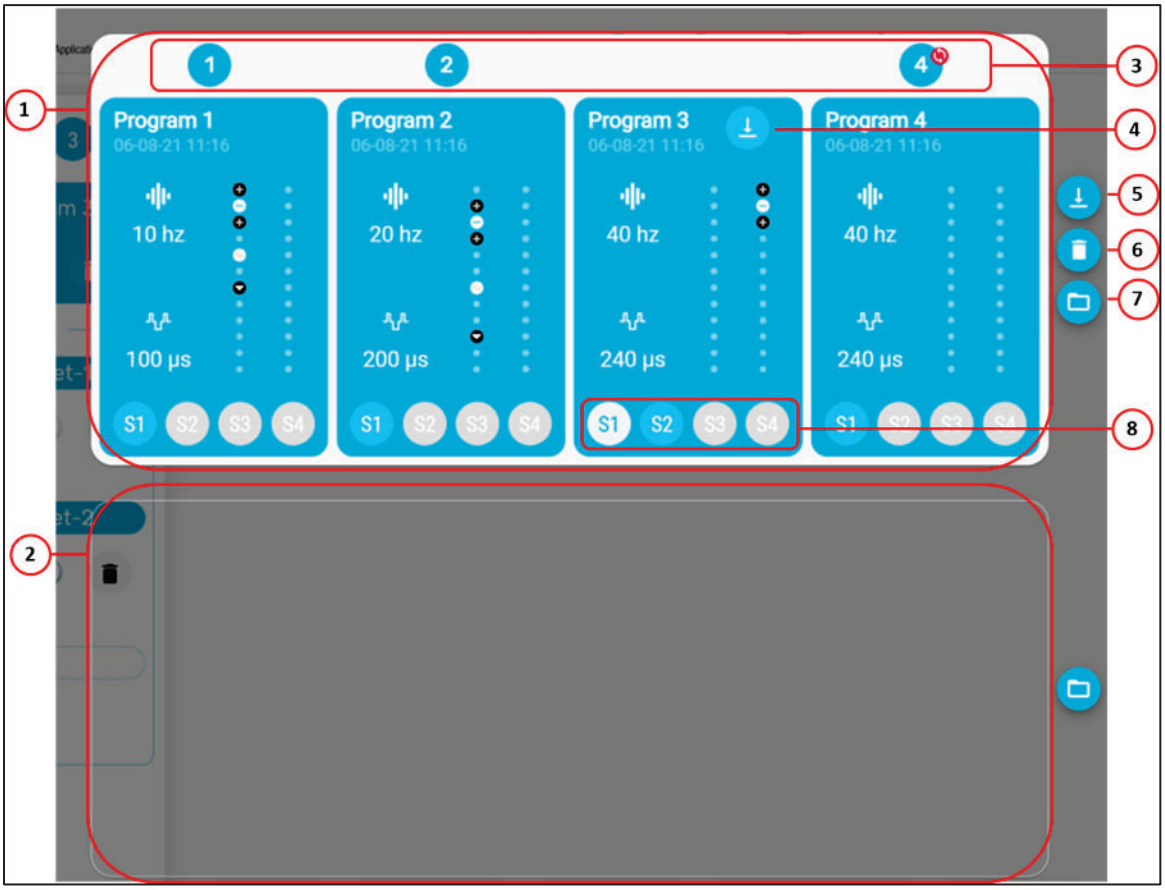


Figure 6.25: Layout of the SaveSlot window.

1. SaveSlot #1
2. SaveSlot #2 (scroll down to see the other 3 SaveSlots)
3. Indicators of Synchronization
4. Load Program/Stim-Set button
5. Load (all) Programs button
6. Delete SaveSlot button
7. Load SaveFile button
8. Stim-Set selector

When viewing the SaveSlots, numbers above each program (Indicators of Synchronization) indicate programs on the CPA that match what's saved in the SaveSlot. If the program on the CPA does not match exactly the program that's on the stimulator, then a sync icon will also appear (for example, see Program 4 in Figure 6.25).

2. … Into a file in the SaveFile folder for the visit.

   Programs are saved automatically into a SaveFile after connection and upon disconnection, and any time you save programs manually.

   SaveFiles are stored in the SaludaData folder for this session (see Section 6.7.1.1).

To save programs:

1. Access the Program Management tab.

2. Touch the Save Programs button .
   This will save the entire set of programs into the next available SaveSlot and into a SaveFile.

6.4.3.5 *Load a Program/Programs from memory*

From within the Program Management tab, with stimulation off, you can load previously saved programs into your programming session from a SaveSlot, or from a SaveFile (via a SaveSlot).

From SaveSlots (within the CPA):

1. Touch the Program label to access the SaveSlots menu (Figure 6.25).
2. a. Select the group of programs you want to download, and touch the adjacent 'Load (all) Programs' button . This will overwrite all 4 programs displayed on the CPA.
   or
   b. Select the specific program you want to download from within a SaveSlot, and touch the 'Download Program' button that appears in that program box. This will only overwrite the program that you selected when you opened the SaveSlot menu.

From SaveFiles:

If you have programs saved on the CI that are not in a SaveSlot (i.e. from a previous day's programming session), you will find these via the 'Load Programs from File' button .

There are two ways to load programs from a SaveFile into a SaveSlot:

1. From within the Program Management tab…
   a. Touch the 'Load Programs from File' button .
   b. Navigate (through the file manager window that pops up) to the file to be loaded.
   c. Click 'Open'. This will load a previously saved program into the next available SaveSlot.
2. From within the SaveSlot menu…
   a. After touching the Program label (to open the SaveSlot menu)
   b. Scroll to the SaveSlot (row) that you want to load the SaveFile into (i.e. an empty one, or one that you want to over-write)
   c. Touch the 'Load Programs from File' button next to the selected SaveSlot.

6.4.3.6 *Add a Stim-Set*

From within the Program Management tab (Figure 6.23),

1. Select the Program number to edit.
2. Touch the 'Add Stim-Set' button. 

6.4.3.7 *Remove a Stim-Set*

1. You can delete a Stim-Set by touching the Delete button  within the corresponding Stim-Set box. You cannot delete Stim-Set-1.
2. You can disable/enable a Stim-Set with the toggle  in the corresponding Stim-Set box. You cannot disable Stim-Set-1.

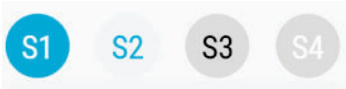
6.4.3.8 *Change which Stim-Set is used for measurement*

Stim-Set-1 is the Stim-Set that contains measurement electrodes. To change which Stim-Set to use for ECAP measurements:

1. Access the Program Management tab.
2. Touch and hold the label for the Stim-Set that you want to use.
3. Drag it to the top (until it's over Stim-Set-1) and release.

6.4.3.9 *Select the Stim-Set to view and/or configure:*

From within any other tab (outside of the program management tab), select a Stim-Set number (S1, S2, S3, or S4). These appear in place of the program numbers that appear when you're in the program management tab.



- White font on a colored (blue or orange) background represents the currently selected Stim-Set (e.g. S1 in the example above).
- Colored font on a light grey background represents an enabled Stim-Set that's not currently selected (e.g. S2 in the example above).
- Black font on a darker grey background represents a Stim-Set that has been enabled and then disabled, and it will be re-enabled if you select it (e.g. S3 in the example above).
- White font on a darker grey background represents a Stim-Set that is empty, and cannot be selected (e.g. S4 in the example above).

6.4.3.10 *Load a Stim-Set from memory*

You can load a single Stim-Set from a SaveSlot into any Stim-Set of a Program.

1. Touch the Stim-Set label for the Stim-Set to be over-written. This will take you to the SaveSlots menu.
2. Select the specific program you want to download a Stim-Set from.
3. Select the specific Stim-Set within the selected program that you want to download.
    - When it has been selected, the Stim-Set Selector will have a colored background

with white font (e.g. S2 in the example below).

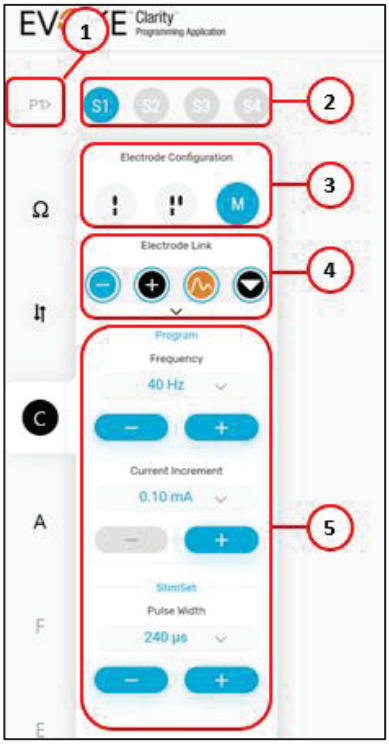
- An empty Stim-Set will have a grey background (e.g. S3 and S4 in the example below).



4. Touch the 'Download Stim-Set' button  that appears in that program box. This will overwrite the Stim-Set that you selected when you opened the SaveSlot menu.

6.4.4 Coverage Tab

a. Touch the **Coverage** tab on the left column navigation. It is recommended that the **Electrode**, **ECAP**, and **Current (mA)** displays are selected to view on the CPA screen.



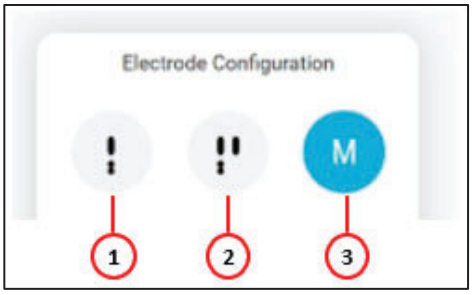
1. Program Number
2. Stim-Set Number
3. Electrode Configuration
4. Electrode Link
5. Program and Stim-Set parameters

Figure 6.26: Coverage Tab Layout.

b. Stop stimulation  if Stimulation is running.

c. Note the Program Number and Stim-Set number that's currently selected next to the Program management tab (i.e. P1> S1 in the above figure).

d. Choose how you would like to select the stimulation electrodes using the options under Electrode Configuration.



1. Automatic Single Lead
2. Automatic Dual Lead
3. Manual

Figure 6.27: Electrode Configuration options.

3. For **Automatic Single Lead** electrode configuration, touch the electrode you want to use as the cathode in the Electrode display. Touch on the cathode again to cycle through electrode configurations. The CPA will automatically select the recording and reference electrodes for you.

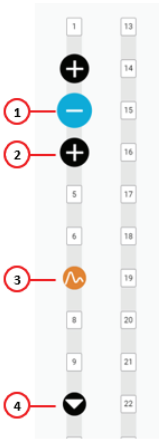
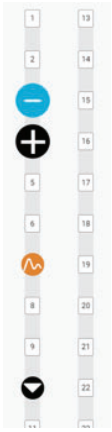
Tripolar: Single lead	Bipolar: Single lead
	

Figure 6.28: Automatic Single Lead.

1. Cathode (Stimulating electrode)
2. Anode (Return electrode)
3. Recording electrode
4. Reference electrode

4. For **Automatic Dual Lead** electrode configuration, touch the electrode you want to use as the cathode in the Electrode display. Touch on the cathode again to cycle through configurations. The CPA will automatically select the recording and reference electrodes for you.

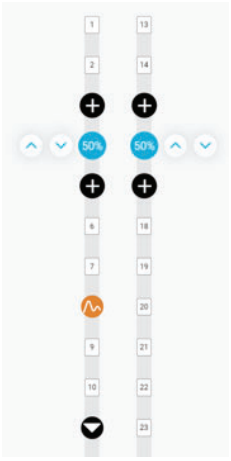
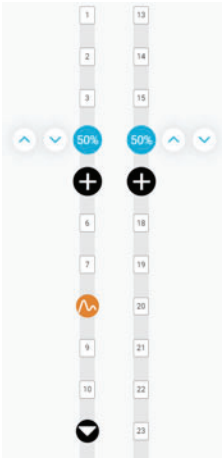
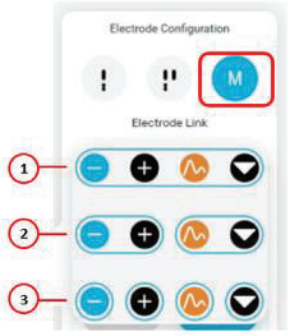
Tripolar: Dual lead	Bipolar: Dual Lead
	

Figure 6.29: Automatic Dual Lead.

5. Current steering is available whenever there is more than one cathode, to balance the strength of paresthesia felt in different areas of the patient's body.
   - The cathodes will now be displayed with a % value and ^ v icons.
   - The % value represents the % of the total current going to that cathode.
   - To deliver more current to a cathode touch the ^ icon. To deliver less current to a cathode touch the v icon. The % of current delivered at the other cathodes will automatically adjust to keep the total at 100%.
6. For **Manual** electrode configuration, you can manually change, add, or remove electrodes by selecting the electrode you wish to change, then choosing if you want to remove it, or change it to a cathode, anode, recording, or reference electrode.

   To move selected electrodes, there are three options that can be used for Manual electrode configuration (Figure 6.30):



1. Link all
2. Link only stimulation and link only Measurement
3. Independent electrode selection

Figure 6.30: Electrode Link.

- **Link all** – Moves cathode, anode, recording, and reference electrodes together. When you select and drag one of them to a new electrode location in the Electrode display.
- **Link only Stimulation and link only Measurement electrodes**
  a. Moves cathodes and anodes together when you select and drag either a cathode

or anode to a new electrode location on the Electrode display.

b. Moves recording and reference electrodes together when you select and drag either a recording electrode or reference electrode to a new electrode location on the Electrode display.

- **Independent electrode selection** – Allows you to move anode, cathode, recording, and reference electrodes individually to any new electrode location on the Electrode display.

7. All settings are set to default values for new programs. You can adjust the individual stimulation parameters in order to adjust paresthesia coverage (e.g. Pulse Width) and/or different sensation (e.g. Stimulation Frequency) by touching on "Advanced" within the **Program and Stim-Set Parameters** in the **Coverage** tab (see Figure 6.31).
   - To set standard stimulation parameters when reprogramming existing programs, go to the **Program Settings** tab → *Advanced* → touch the *Reset* button under "*Reset Program to Defaults*."
8. Restart stimulation with the new stimulation configuration.

   Note: You cannot change the cathode or anode electrodes while stimulation is running.

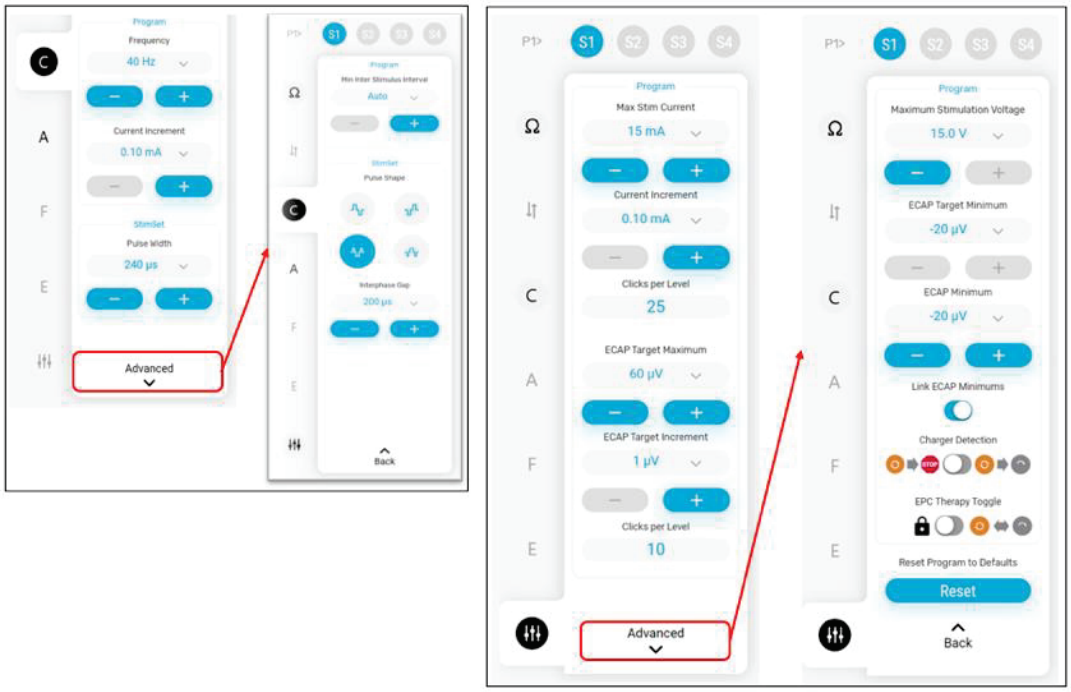
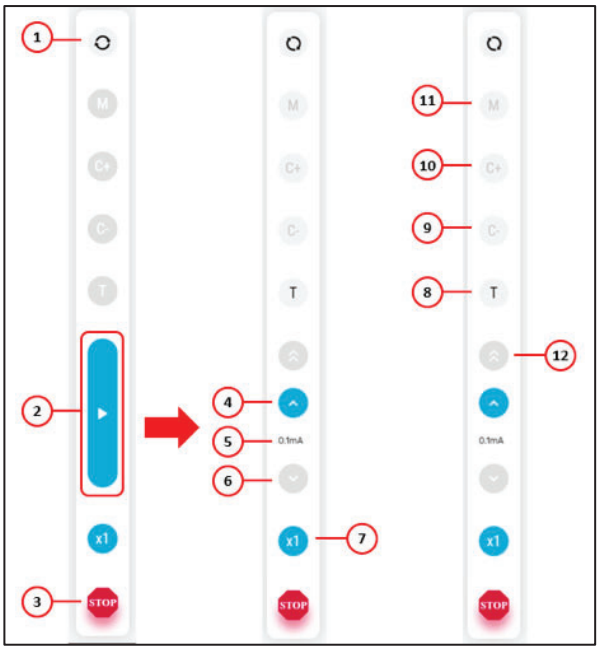


Figure 6.31: Default values for new programs within **Program and Stim-Set Parameters** in the **Coverage** tab (Left) and the **Program Settings** tab (Right).

6.4.4.1 *Start and stop stimulation*

1. Touch on the Start Stimulation button (see Figure 6.32) on the right control panel of the **Programming** page to start stimulation.



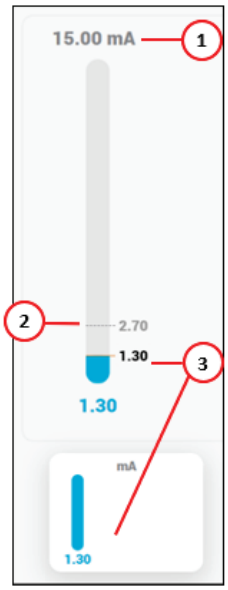
1. Enable or Disable Closed-Loop stimulation
2. Start stimulation
3. Stop stimulation
4. Increase current
5. Current increment
6. Decrease current
7. Multiply current increment
8. Threshold
9. Comfort Minus
10. Comfort Plus
11. Maximum
12. Ramp up

Figure 6.32: Right Control Panel on the Programming page, with Start Stimulation button and stimulation controls. With Closed-loop disabled, buttons on the screen will turn **blue** to indicate they are active.

Note: The ECAP and Current (mA) thumbnails will become active, e.g. they will update continuously with the ECAP amplitude and current setpoint. When Closed-loop is enabled, they will show the ECAP target and the stimulation current respectively.

2. Touch the *Increase current* button to increase stimulation current to the desired level (mA).
3. Touch the *Decrease current* button to decrease stimulation current.
4. Touch the *Stop* button STOP to stop stimulation at any time.

   Note: The current will increase/decrease by the current increment (mA) set in **Program and Stim-Set Parameters**. Touch the **Multiply current increment** button x1 to increase the current increment by up to 2x. The current scale is shown in the **Current (mA)** display. The scale will extend to the maximum current set in the **Program and Stim-Set Parameters** tab (see Figure 6.33).



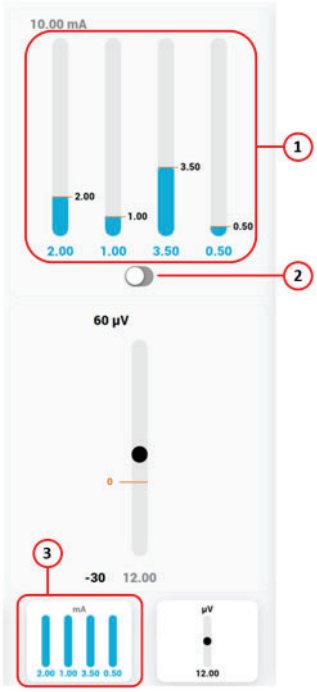
1. Max Stim Current setting
2. Previous current level (when stimulation was last stopped)
3. Current set point (mA) (desired level)
4. Active Current level (mA) (which lags set point)

Figure 6.33: Current (mA) display (top) and thumbnail (bottom).

6.4.4.2 *Interleaved stimulation*

A program may contain several interleaved stimulation sets (Stim-Sets), targeting several areas of pain. The CPA has the ability to concurrently run up to four (4) Stim-Sets per program. Refer to Section 6.4.3 Program management Tab for details on how to setup, configure, and change Stim-Sets.

The first Stim-Set (S1) is the one with which measurements are made. It is the only one that can contain measurement electrodes.



1. Current bars in the current display—one for each Stim-Set that is enabled.
2. Stim-Set Group toggle
3. Current thumbnail—with set point levels for each Stim-Set

Figure 6.34: UI elements related to Interleaved Stimulation.

Note: Enable the Stim-Set Group toggle to group the Stim-Sets so that current changes for all Stim-Sets concurrently.

- If disabled (to the left), then only the Stim-Set that is currently selected will change.
- If enabled (to the right), Stim-Sets are grouped. This is the default.

Set up interleaved stimulation

To set up multiple Stim-Sets in a program:

1. Start with the first Stim-Set (SS1). When you first setup a program, you are working with S1.
2. Create a second Stim-Set (e.g. S2), or as many Stim-Sets as you need, via the Program management tab (see Section 6.4.3).
3. Ungroup the Stim-Sets.
4. For each Stim-Set:
    a. Select the Stim-Set number at the top of the left panel.
    b. Configure the stimulation settings in the C tab (see Section 6.4.4 Coverage Tab).
    Note: Frequency, maximum current, and current increment are equal across stimulation sets, while pulse width may be set independently.
    c. Note the threshold level.
5. After configuring each Stim-Set, set their relative levels.
    a. Select the Stim-Set number at the top of the left panel.
    b. Increase current to the threshold level noted above.

6. After setting each Stim-Set current to their respective threshold levels, group the Stim-Sets using the Stim-Set Group toggle.
7. Increase current (with Stim-Sets grouped now) to the desired level.
8. Measurement is only enabled for the first stimulation set (S1). The ECAP measurement and closed-loop settings from the first stimulation set are used for closed-loop control of all stimulation sets.
   To change which electrode configuration is associated with the measurements, see Section 6.4.3.8.
9. Complete the ECAP acquisition, filter fitting, and evaluation steps as you would for a program with no interleaving.

   Note: Closed-loop stimulation will only operate based on the settings in the first Stim-Set. The closed-loop control will vary the current to each Stim-Set such that the ratio of current between Stim-Sets remains constant.

Enable/Disable a stimulation set in a program

To enable/disable a Stim-Set in a program: See 6.4.3.9 in Program Management tab.

Things to be aware of when enabling/disabling a Stim-Set:

- When a Stim-Set is disabled, the Stim-Sets that are still enabled will continue to increase/decrease at the previous ratio.
- If a stimulation set is disabled its ratio will be set to 0 and it will need to be reconfigured.

Changing the ratio between Stim-Sets

The ratio between Stim-Sets can be changed, even during stimulation.

1. Ungroup the Stim-Sets (using the Stim-Set Group toggle).
2. Select a Stim-Set number to be adjusted and change the current to the new desired level.
3. Re-group the Stim-Sets (using the Stim-Set Group toggle) and continue stimulation as normal.

6.4.5 Acquisition Tab

Touch the **Acquisition** tab to start setting up an optimal ECAP measurement. It is recommended that the **Electrode** and **ECAP** displays are selected to view on the CPA screen (see Figure 6.35).

The stimulator records the ECAP signal and displays a plot of the ECAP on the **ECAP** display. ECAP measurement is only possible for stimulation frequencies of 200 Hz or less (250 Hz or less for Amplitude option). ECAPs can only be generated and measured above a minimum (threshold) current, which varies with different postures and between patients.

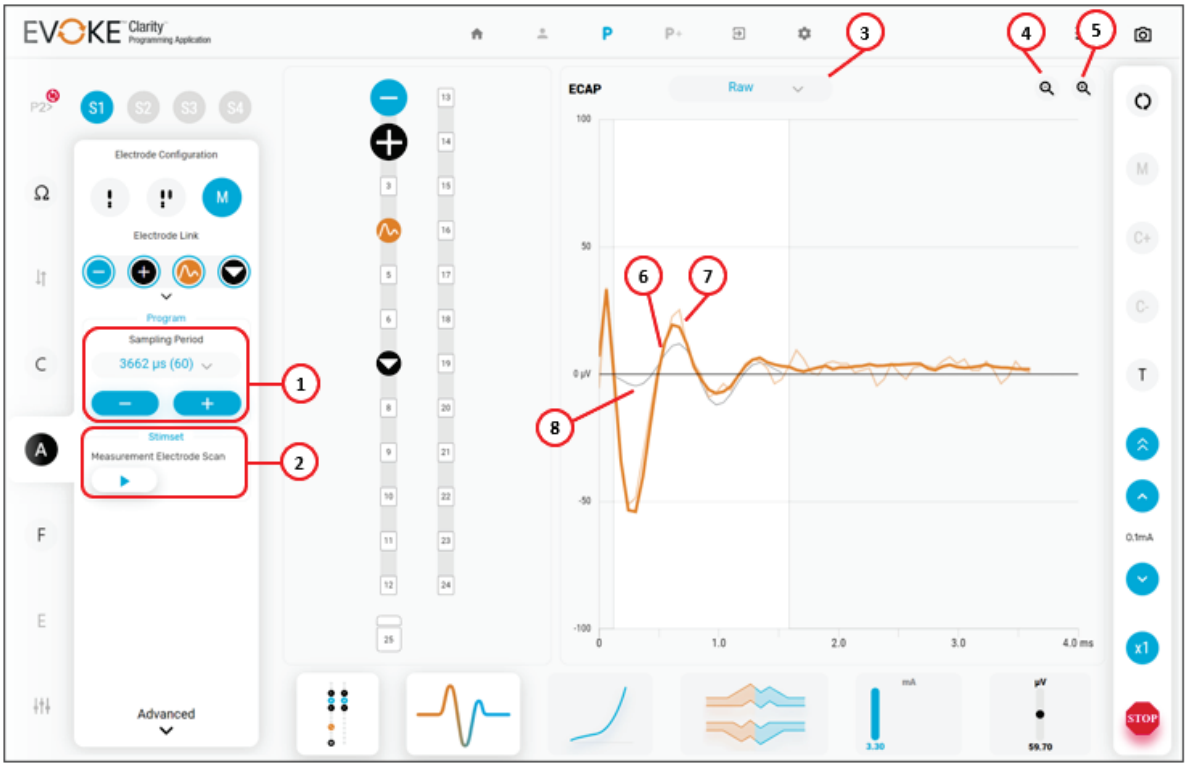


Figure 6.35: Acquisition tab with Electrode and ECAP displays visible

1. Sampling Period
2. Measurement Electrode Scan (MES) start/stop
3. ECAP display mode
4. Zoom out (Y-scale)
5. Zoom in (Y-scale)
6. Average ECAP signal (thick orange)
7. Instantaneous ECAP signal (thin orange)
8. Correlation Filter used to measure (black)

When stimulation is running, a measurement electrode scan (MES) of up to 4 different measurement electrode configurations may be displayed on the ECAP display. Refer to Section 6.4.5.3 for more information on using MES to optimize the choice of measurement electrodes and settings.

To optimize the ECAP measurement:

1. Start stimulation and increase the stimulation current so that a clear ECAP signal is visible and/or above the patient's perception threshold.
2. Use the ECAP display and measurement electrode scan to determine the measurement electrode configuration with the optimal ECAP based on size/shape.
   a. Enabling ClearCAP may improve ECAP measurement (see Section 6.4.5.4 for more information on ClearCAP).
3. Touch and drag the recording electrode to move as needed to optimize the ECAP signal.
4. Touch and drag the reference electrode to move as needed to optimize the ECAP signal.

6.4.5.1 *Settings in Acquisition and Acquisition → Advanced*

See Section 7.3 for more information about each setting.

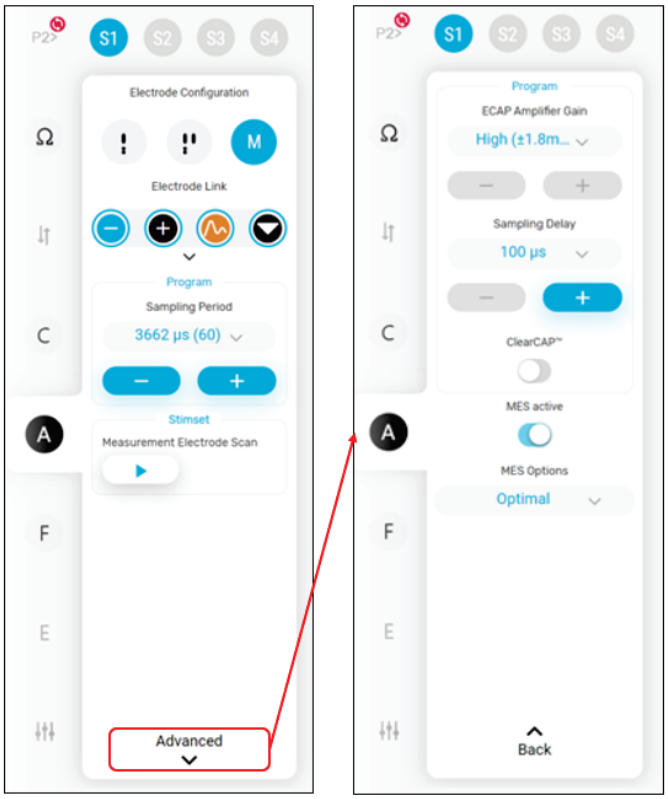


Figure 6.36: Acquisition tab and the Advanced options.

a. **Sampling Period**

   The number of samples of the signal to record. The Sampling Period must be greater than or equal to the Processing Offset plus the Processing Period. Consider increasing this if the ECAP signal cannot be optimally measured (i.e. the filter cannot be optimally aligned and/or the complete ECAP signal cannot be seen in the ECAP display).

b. **Sampling Delay**

   The amount of time for the system to wait, following the stimulus pulse, before recording the signal. Consider increasing this from default (100 µs) if the Processing Offset cannot be increased enough for optimal measurement of the ECAP.

c. **ECAP Amplifier Gain**

   The voltage range of the signal that can be recorded. The default setting is 'High (± 1.8mV)'. Consider setting this to 'Low (± 7.2 mV)' if the ECAP signal is clipping.

d. **MES Toggle and MES Options** (see Section 6.4.5.3).

e. **ClearCAP** disable/enable (see Section 6.4.5.4).

6.4.5.2 *ECAP display and artifact estimation*

The signal recorded by the stimulator is a combination of the ECAP, artifact from the stimulation pulse, and background electrical or neural noise. The artifact is a signal resulting from the

stimulus pulse that is not related to neural activity, but can interfere with measurement of an ECAP.

The CPA estimates the ECAP and artifact from the recorded signal so that an ECAP estimate may be displayed with the artifact and noise removed.

The ECAP display shows signals from up to 4 measurement configurations represented by 4 colors (see Section 6.4.5.3). The display shows the 'latest' from one stimulation, 'average' from 16 of those measurements and an 'estimate' of the artifact component of the signals.

Select the drop-down menu at the top of the ECAP display to select amongst three modes of ECAP display: Raw, Scrubbed (simple) and Scrubbed (detailed).

A) **Raw**

- latest recorded signal (light line)
- average recorded signal (dark line)
- average artifact estimate (thin line)

B) **Scrubbed (simple)**

- average ECAP estimate (dark line)

C) **Scrubbed (detailed)**

- latest ECAP estimate (light line)
- average ECAP estimate (dark line)
- average recorded signal with average artifact estimate subtracted (dashed line)

6.4.5.3 *Measurement electrode scan (MES)*

The ECAP display shows the average ECAP estimate for each measurement electrode configuration and the correlation filter used to measure the ECAP. The ECAP display shows the currently in use (orange) and additional recommended (blue, green, purple) recording and reference electrode configurations.

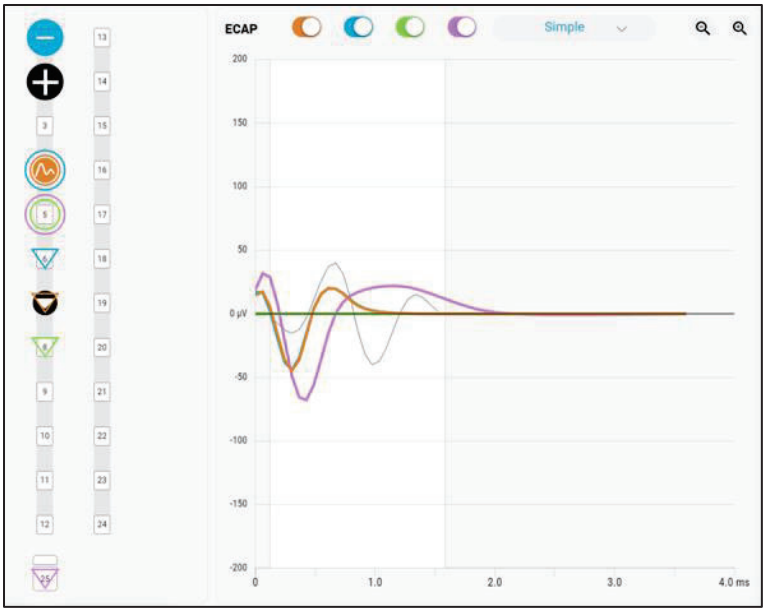


Figure 6.37: ECAP display and Electrode display showing the currently in use measurement electrode configuration (orange) and 3 other configurations (blue, green, purple).

MES allows ECAPs from multiple measurement electrode pairs to be displayed on the ECAP display (Figure 6.38) at the same time. It is intended to assist in optimizing the choice of measurement electrodes. By default, MES will automatically start when stimulation is started.

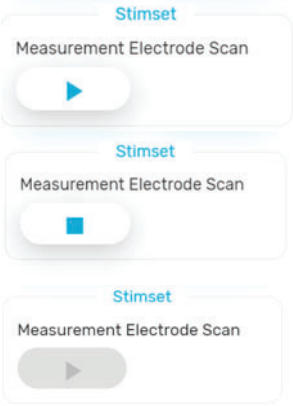
MES displays up to four configurations: the configuration programmed by the user, and up to 3 other configurations recommended by the system. Each can be added/removed from the display using the toggles at the top of the ECAP display when it is maximized.

The measurement electrodes used in the scan are based on the location of the stimulation electrodes, as well as the recording and reference electrodes that have been programmed by the user.

The recommended measurement settings are calculated from the average recorded signal when the ECAP display is in the raw mode and from the ECAP estimate when in the scrubbed modes.

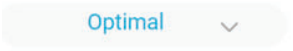
To enable MES:

- The programmed stimulation and measurement electrodes must be on the same lead.
- Neither of the measurement electrodes can be adjacent to a stimulation electrode.
- A measurement electrode cannot be on the case (E25).
- The recording electrode must be between the stimulation and reference electrodes

Button	Action
	Stop or Start the measurement electrode scan while stimulation is running. This does not change the automatic start of the scan when stimulation is started. *Note these buttons are greyed out if MES is disabled.

MES settings

1. Within the Acquisition tab, Touch Advanced to open additional setting options.

Button	Action
	Choose the method used to select up to 3 electrode configurations to be used in the scan These configurations are in addition to the user selected configuration (for examples see):

Button	Measurement	Reference
*Optimal** (#electrodes from stimulation/cathode)	3 3 4 4	5 6 7^{+} case (E25)
*Fixed Reference^* (#electrodes from selected)	1 closer‡ 1 further 2 further	As selected
*Fixed Measurement^* (#electrodes from selected)	As selected	1 closer 1 further 2 further
*Fixed Distance^* (#electrodes from selected)	1 closer‡ 1 further 2 further	1 closer 1 further 2 further

Button	Action
	Disable or Enable the measurement electrode scan for the duration of the programming session. When disabled, the measurement electrode scan will not be automatically started when stimulation is started.

***Note:** Default**.** For *Optimal,* if an electrode is disconnected, that configuration will be skipped.

^**Note:** For *Fixed,* if an electrode is disconnected, that configuration will be skipped and the next electrode further from the stimulation electrode will be used until the end of the lead is reached, or the reference electrode is reached for *Fixed Reference*.

⁺**Note:** For this configuration, if the stimulation electrode is on E6 or E7, then the reference electrode will be 6 electrodes from stimulation instead of 7.

‡**Note:** Configurations with the measurement electrode adjacent to the stimulation electrode will be skipped.

Optimal				*Fixed Reference*				*Fixed Measurement*				*Fixed Distance*			
+E6	+E5	+E5	+E6	+E6	+E5	+E7	+E8	+E6	+E6	+E6	+E6	+E6	+E5	+E7	+E8
-E9	-E7	-E8	-E25	-E9	-E9	-E9	-E9	-E9	-E8	-E10	-E11	-E9	-E8	-E10	-E11

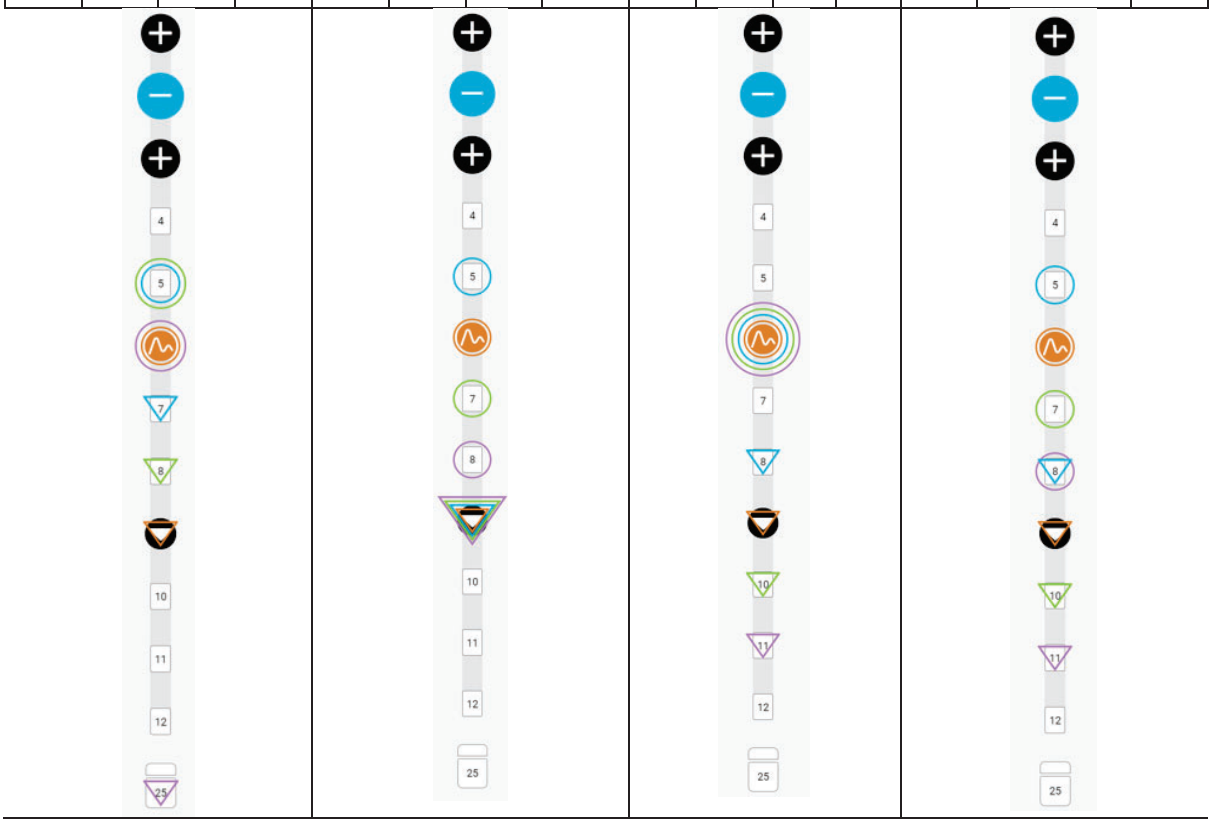


Figure 6.38: Examples of Measurement Electrode Scan position configuration methods when the stimulation electrode (cathode) is at E2.

6.4.5.4 ***ClearCAP***

ClearCAP is used to reduce the artefact recorded during measurement by cancelling the artefact from the stimulation and return electrodes; this feature is best used when optimizing ECAP measurement. The Reference electrode is colored differently (with a blue triangle) when ClearCAP is enabled, however, the measurement functionality of the Reference electrode remains unchanged. ClearCAP may be enabled or disabled for each program.

Note: ClearCAP cannot be enabled or disabled during stimulation.

Caution: The case electrode (E25) should not be used as the Reference electrode if ClearCAP is enabled.

Caution: If the Measurement or Reference electrode is within 2 electrode spacings from a stimulation or return electrode, ClearCAP may not perform optimally.

In order to assess performance, comparing stimulation with and without ClearCAP (all other settings unchanged), ensure the following are true:

- Artefact magnitude should be reduced with ClearCAP enabled (see Figure 6.39).
- ECAP amplitude variability should be unchanged or reduced with ClearCAP enabled.
- Criteria described elsewhere in this section are still met with ClearCAP enabled.

  Note: If the criteria above cannot be met, ClearCAP should be disabled for the current program configuration.

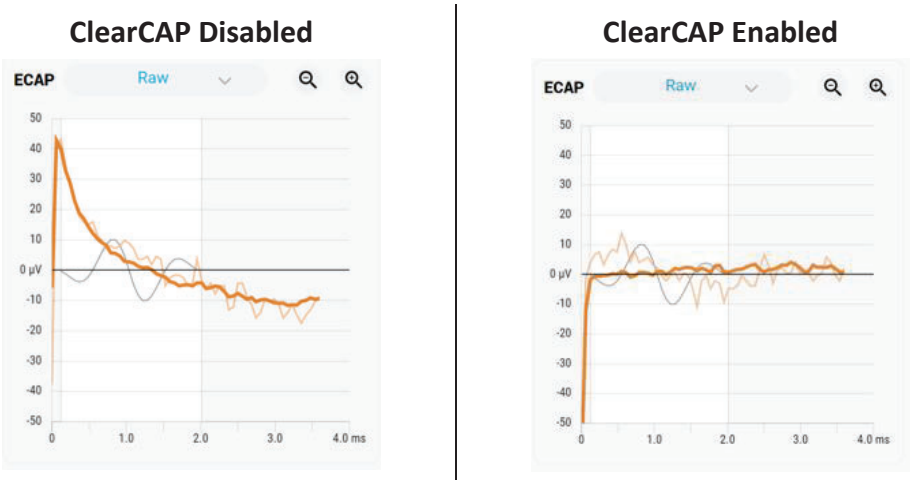
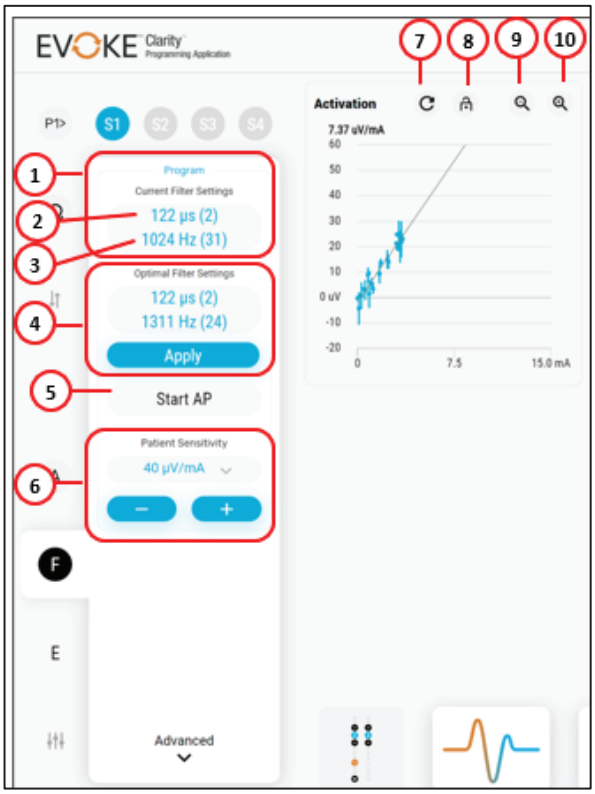


Figure 6.39: ECAP Display showing an example of artefact magnitude with ClearCAP disabled and subsequently decreasing when ClearCAP is enabled.

6.4.6 Filter Tab

Touch on the **Filter** tab on the left column navigation to fit the filter and amplify the ECAP signal by reducing artifact and noise. It is recommended that the **Activation Plot**, and **ECAP** displays are selected to view on the CPA screen.



1. Current Filter Settings
2. Processing Offset
3. Filter Frequency
4. Optimal Filter Settings
5. Start AP (Activation Plot)
6. Patient Sensitivity
7. Clear AP
8. Lock AP
9. Zoom out
10. Zoom in

Figure 6.40: Filter tab layout.

1. Touch the ***Apply*** button to set the optimal filter settings for processing offset and filter frequency.
2. Ensure the applied (current) filter settings match the recommended optimal filter settings (Figure 6.41), and check that the peaks of the ECAP signal line up with the peaks of the correlation filter. If they don't, you may manually adjust Processing Offset and Filter Frequency until they do.

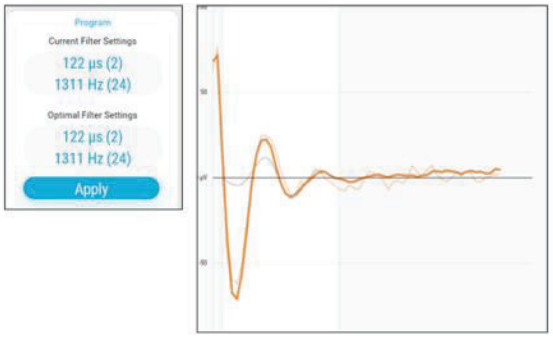


Figure 6.41: ECAP display with a well-matched filter (-).

Note: The default filter has a negative first peak (Figure 6.41). In some cases, filter alignment may be improved by flipping the filter the first peak is positive. This is done by changing the measurement type to 'Filter (+)' from the Measurement Type dropdown in Filter Tab → Advanced (Figure 6.42).

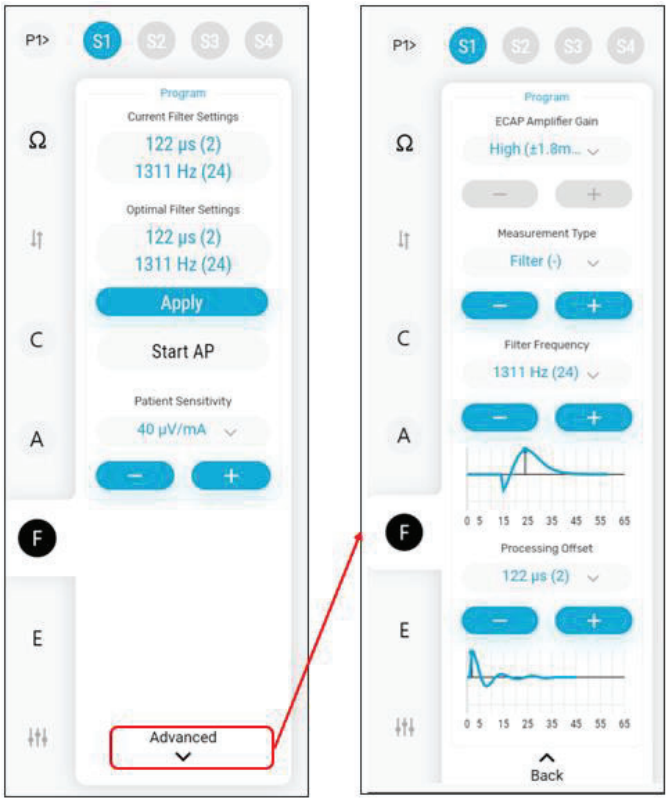


Figure 6.42: Filter Tab → Advanced.

3. To manually adjust the processing offset and filter frequency go to Filter Tab→Advanced. The blue dot on the plot is the recommended (peak of plot), while the black line is the setting in use.
4. There are four measurement type options in Filter Tab → Advanced (Figure 6.42):

a. ECAP Sampling Disabled

The ECAP recording is disabled for stimulation frequency greater than 250Hz. This option is not available for stimulation frequency less than or equal to to 250Hz

b. ECAP Measurement - filter (+)

The ECAP amplitude is measured using a correlation filter with peaks aligned with the ECAP signal. The first peak is positive and the Processing Period and Filter Frequency are adjusted to align the filter. The ECAP signal is also recorded and displayed in the ECAP display. For this option, closed-loop may be enabled, and stimulation frequency is available up to 200Hz.

c. ECAP Measurement - filter (-) [default setting]

The ECAP amplitude is measured using a correlation filter with peaks aligned with the ECAP signal. The first peak is negative and the Processing Period and Filter Frequency are adjusted to align the filter. The ECAP signal is also recorded and displayed in the ECAP display. For this option, closed-loop may be enabled, and stimulation frequency is available up to 200Hz.

d. ECAP Measurement - Amplitude

The ECAP amplitude is measured from the peak-to-peak amplitude of the ECAP signal within the Processing Period, aligned such that it contains the ECAP peaks and there will be no optimal filter settings. For this option, closed-loop may be enabled, and stimulation frequency is available up to 250Hz.

Note: This option should only be used with closed-loop enabled where the peak-to-peak amplitude is not affected by artefact.

6.4.6.1 *Measure activation plot and therapeutic window*

The settings for closed-loop stimulation vary between patients and for different electrode configurations. These settings depend on the sensitivity of the ECAP to changes in current.

The CPA can measure ECAP sensitivity as the current is varied in the Activation Plot display, following these steps:

1. Ensure you have optimized the ECAP measurement (refer to Section 6.4.6).
2. Measure the Activation Plot.
   a. Mark the activation plot levels by touching the following buttons (see Figure 6.43):
      - *Threshold* (**T**): ECAP threshold or when the patient first feels a change in sensation (e.g. paresthesia or pain relief).
      - *Comfort* (**C-** and **C+**): When the patient reports a preferred comfortable sensation, for increasing or decreasing stimulation, respectively.
      - *Maximum* (***M***): When the patient could tolerate stimulation for no more than approximately one minute.

      Note: When marked, the button turns blue.

Note: The levels will be indicated by horizontal lines on the Current (mA) and ECAP Amplitude (µV) displays, and horizontal (ECAP amplitude) and vertical (current) lines on the activation plot display (Figure 6.43). They will also be recorded as notes in the programming data, and screenshots in the Notes window.

3. The therapeutic window is defined by the difference between the ECAP amplitudes at Threshold (T) and Maximum (M). Only enable closed-loop if the therapeutic window is > 10 µV.
4. To change the levels, touch the button once to clear the mark, then touch again to set the mark to the new level.

   Note: The Threshold level must be less than all other levels and the Maximum level must be greater than all other levels. If an activation plot level is selected that causes a previously selected level to fall outside these criteria, then the previously selected mark will be cleared (e.g. If **C+** is selected at a level less than **T**, then the mark for **T** will be cleared).

   Note: The levels will be cleared if settings are changed that could affect the activation plot levels (e.g. if pulse width is changed, stimulation current and ECAP amplitude levels will be cleared; if processing offset or filter frequency are changed only ECAP amplitude levels will be cleared).

   b. Touch the *Ramp Up* button to gradually increase the stimulation current or ECAP Target to the next activation plot level or the level when stimulation was last stopped.

   Caution: If the patient reports that stimulation is getting stronger than expected due to, for example, a change in posture:

   - Stop stimulation by pressing the *Stop* button, or
   - Stop the ramp up by pressing the *Increase* or *Decrease* buttons.

   Note: The CPA cannot ramp to the **M** level that was set.



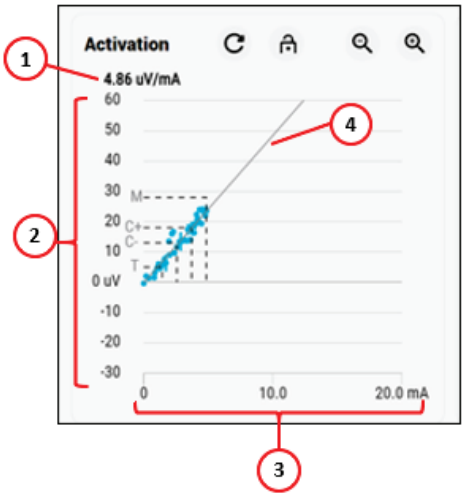
Figure 6.43: Filter Tab with Activation, ECAP Amplitude, Current Amplitude, and ECAP display. The **Ramp Up, M, C+, C-** and **T** buttons are on the right control panel.

5. The activation plot display shows the ECAP amplitude as a function of current, and the measured sensitivity is displayed on the plot (Figure 6.44).
6. Ensure that the displayed activation plot meets the following criteria:
    a. The activation plot should show an obvious inflection in the ECAP amplitude close to the patient's paresthesia threshold. Above this inflection the ECAP amplitude should increase linearly with the stimulation current.
    b. The therapeutic window should be >10 µV.
    c. The measured sensitivity should be >10 µV/mA.

    Note: If a Measured Sensitivity value does not appear then decrease the current increment and repeat steps 2-4 above.

⚠**Caution:** Closed-loop may not operate as intended if the activation plot does not meet these criteria. Do not enable closed-loop operation until the above criteria are satisfied.

7. If the activation plot does not meet the above criteria you will need to improve the signal quality by adjusting the ECAP measurement settings (see Section and 6.4.6) and/or adjusting the stimulation settings (see Section 6.4.4).



6. Measured sensitivity
7. ECAP measurement axis (µV)
8. Stimulator output current axis (mA)
9. Estimated slope of AP (gray line)

Figure 6.44: Activation Plot (AP) Display.

8. If the criteria for the activation plot are met, select the patient sensitivity value that is closest to the measured sensitivity value, rounded up in the Filter tab. The minimum patient sensitivity is 14 µV/mA.

6.4.7 Evaluation Tab

Touch on the **Evaluation** tab once all the settings for the program have been set up and the criteria for the activation plot have been met to evaluate closed-loop operation. It is important to test the effectiveness of the closed-loop control with the patient in various postures.

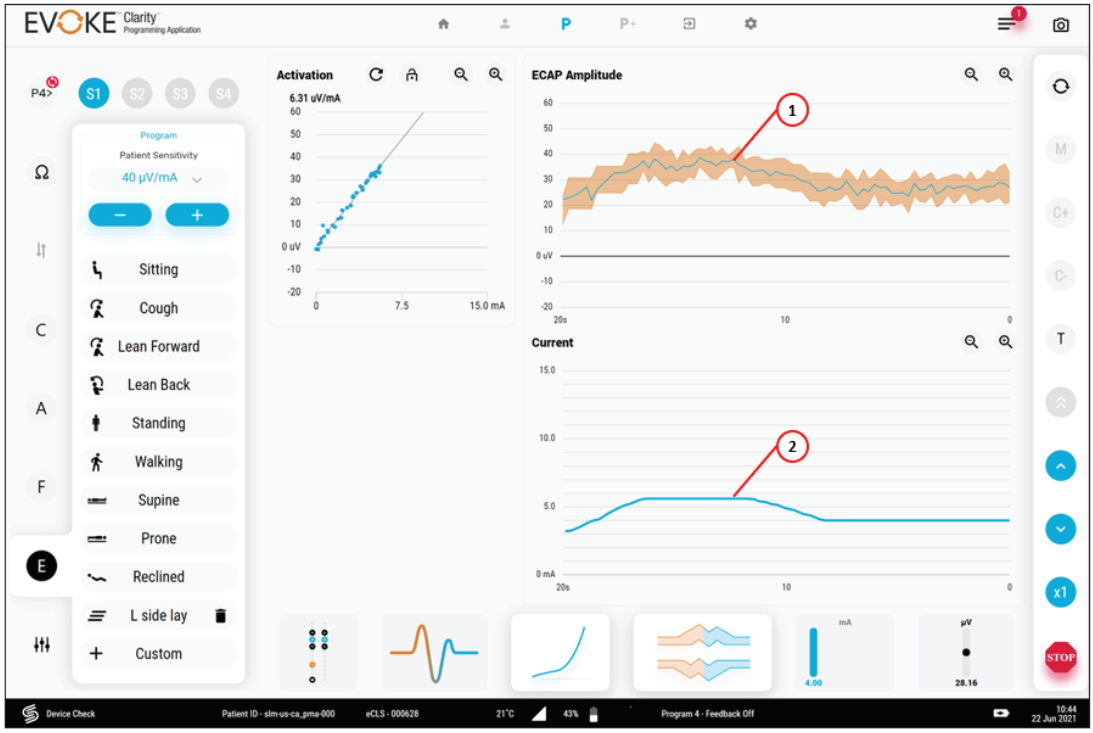


Figure 6.45: Evaluation Tab with Rolling Plot and Activation Plot display. Closed-loop is disabled.

1. ECAP rolling plot (blue line in Closed-loop disabled)
2. Current rolling plot (blue line in Closed-loop disabled)

To evaluation the effectiveness of the closed-loop stimulation:

1. Start stimulation and set the current to a comfortable level.
2. Touch the icon to enable closed-loop stimulation on the right control panel. When closed-loop is enabled the icon will turn orange .
3. When closed-loop is enabled, the ECAP amplitude rolling plot and Current rolling plot line graphs will change from **blue** to **orange** (Figure 6.46). Various elements and buttons on the CPA will also turn **orange** to signal that closed-loop is enabled. The current will also vary over time. The ECAP amplitude will vary around the target. If the ECAP variability is increased after closed-loop is enabled:
    a. You may increase the Patient Sensitivity setting to reduce this variability.
    b. If the measured sensitivity is low (near 10 µV) and the stimulation frequency is low (e.g. 10-20 Hz), try increasing the stimulation frequency to reduce the variability. If you change the stimulation frequency, you will need to check the ECAP measurement and re-measure the activation plot (repeat the steps from Section 6.4.6 onwards).

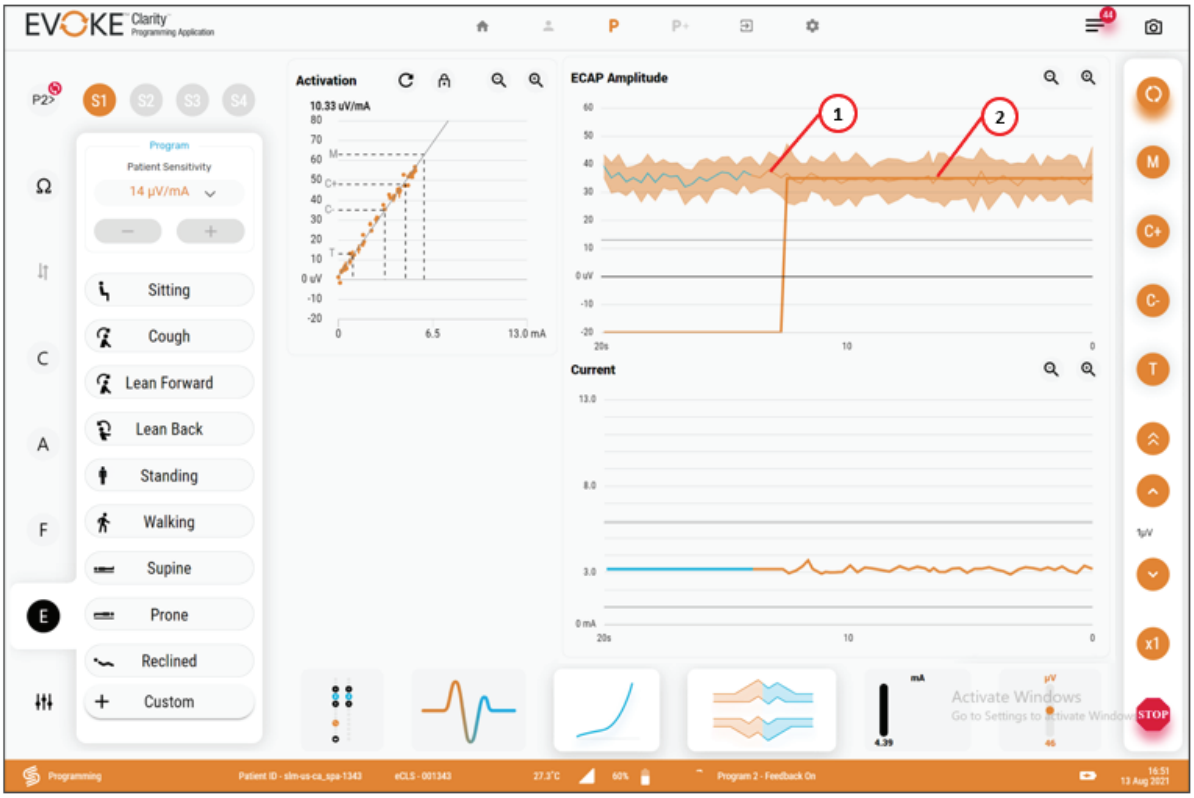


Figure 6.46: Evaluation tab showing transition from closed-looped disabled to closed-loop enabled in the Rolling Plot display.

1. ECAP amplitude rolling plot (thin orange line)
2. ECAP amplitude target (thick orange line)

4. Monitor the rolling plot through various postures. Ask the patient to move into various postures such as sitting, standing and lying on their back (supine) while you watch the rolling plot to see how the closed-loop control responds. The ECAP amplitude will show some variability, but the average ECAP amplitude should track the target level, and changes in current should track the patient's movement (Figure 6.46). If they don't, you may need to adjust the acquisition or filter settings (see Section 6.4.5 and 6.4.6 respectively).
5. During the posture changes, if the patient reports large changes in stimulation intensity when they change postures, you may decrease the Patient Sensitivity setting. If the patient reports discomfort with stimulation sensation while they are not moving, you may increase the Patient Sensitivity setting.

6.4.8 Program Settings Tab

The Program settings Tab includes general program parameters that aren't specific to the CAFE algorithm, which includes limits, increments and intervals.

- Refer to Section 7 for full details about all parameters listed.

6.4.8.1 *Set appropriate limits and increments*

1. Prior to final testing, appropriate limits and increments should be set for each program that the patient has saved to their stimulator.
2. Refer to Table 6.3 for guidelines on determining appropriate values.
3. The limits (both stimulation current and ECAP target minimum and maximum) should be tested to ensure that the stimulator has enough range to allow the patient to receive therapy at a comfortable level across a range of postures (e.g. leaning forward, leaning back, standing, sitting, and walking). If required, the limits should be adjusted accordingly.
4. The increments (stimulation current and ECAP target) should be tested above patient perception threshold to ensure that each step can be felt by the patient. These intervals should not be too large (e.g. significant changes in intensity) or too small (e.g. no noticeable changes in intensity), and adjusted accordingly if required.

   Note: The settings may need to be adjusted following testing of each program.

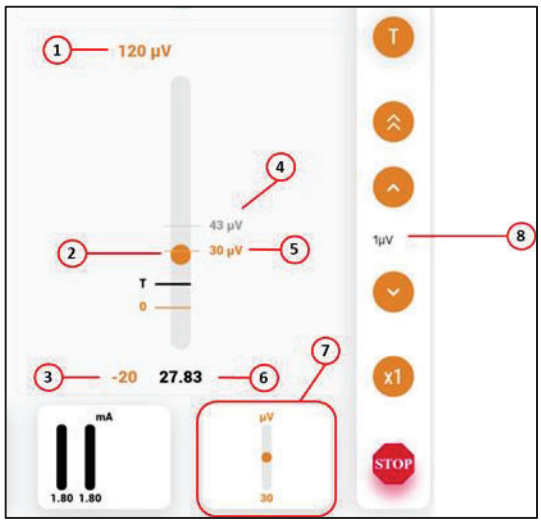
Table 6.3: Guidelines for setting appropriate limits and increments for stimulation current and ECAP target.

Parameter	Guideline
Maximum Current Limit (mA)	Set to the first available value ≥1.5 x stimulation current at the Maximum activation plot level, measured while the patient is in the sitting posture).
ECAP Target Maximum (µV)	Set to the first available value such that the ECAP Target Limit > 0.67*Maximum and ECAP Target Limit > Comfort+, (where Maximum and Comfort+ refer to the activation plot levels measured while the patient is in the sitting posture)
ECAP Minimum (µV)	Set to the highest value such that the ECAP Minimum ≤ minimum ECAP amplitude recorded during collection of the activation plot and posture testing.
ECAP Target Minimum (µV)	Link to ECAP Minimum, or if necessary, de-link and set to the highest value such that the ECAP Target Minimum ≤ ECAP amplitude at the ECAP threshold.
Current Increment (mA)	Set between 0.1 and 0.2 mA, depending on the current range between Threshold and Maximum activation plot levels in the sitting posture. Increase the increment if each step has no noticeable change in intensity for the patient, and decrease the increment if there is too large a change in intensity.

ECAP Target Increment (µV)	Set to the value closest to Comfort+/10 (where Comfort+ refers to the activation plot level measured while the patient is in the sitting posture)

6.4.9 Adjusting stimulation with closed-loop enabled

Closed-loop stimulation may be increased/decreased and stopped using the same controls used when closed-loop is disabled. Rather than controlling the current, these controls will now control the ECAP amplitude target. Touch the Stop button to stop delivery of stimulation current at any time.



1. ECAP Target Maximum
2. Average ECAP amplitude (graphically represented)
3. ECAP Target Minimum
4. Previous Target (when stim was last stopped)
5. ECAP target
6. Average ECAP amplitude (numerically represented)
7. ECAP amplitude thumbnail, with ECAP target (in µV) displayed at the bottom.
8. ECAP target increment.

Figure 6.47: UI elements for ECAP amplitude control.

When the up/down buttons are clicked, the target will increase/decrease by the ECAP Target Increment (µV*)* set in the program settings tab (see Section 6.4.8). The ECAP Target Increment value is shown on the right control panel, between the up and down arrows. The ECAP target is displayed on the ECAP amplitude bar (#5) as well as on the ECAP amplitude thumbnail (#7). The average measured ECAP amplitude is represented on the ECAP amplitude bar by the orange disk (#2), as well as the number at the bottom of the amplitude bar (#6).



6.5 Neurophysiological Measurements Page

The CPA can be used with the eCLS/CLS to measure the neurophysiological characteristics of the patient's spinal cord, such as conduction velocity (CV) and chronaxie and rheobase (CR). These steps detail how to collect data for these measurements, via the Neurophysiological Measurements page.

6.5.1 Setup for neurophysiological measurements

1. Ensure the electrode configuration of the program to be used has been optimized for ECAP measurement.
2. From the Programming page, select any unused program (or any program that you don't plan to load settings from for the neurophysiological measurements). This program will need to be restored after completing these measurements, as will any other programs that you load from within the Neurophysiological Measurements page.
3. Touch **P+** to access the Neurophysiological Measurements page

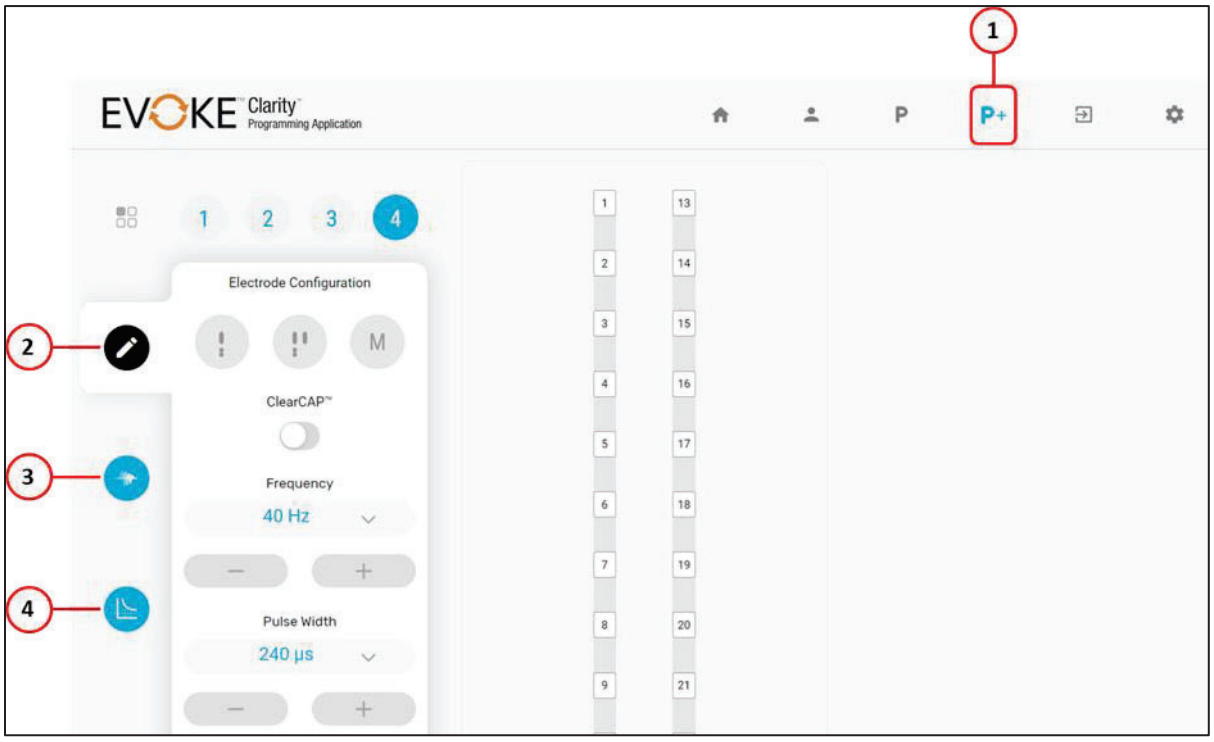
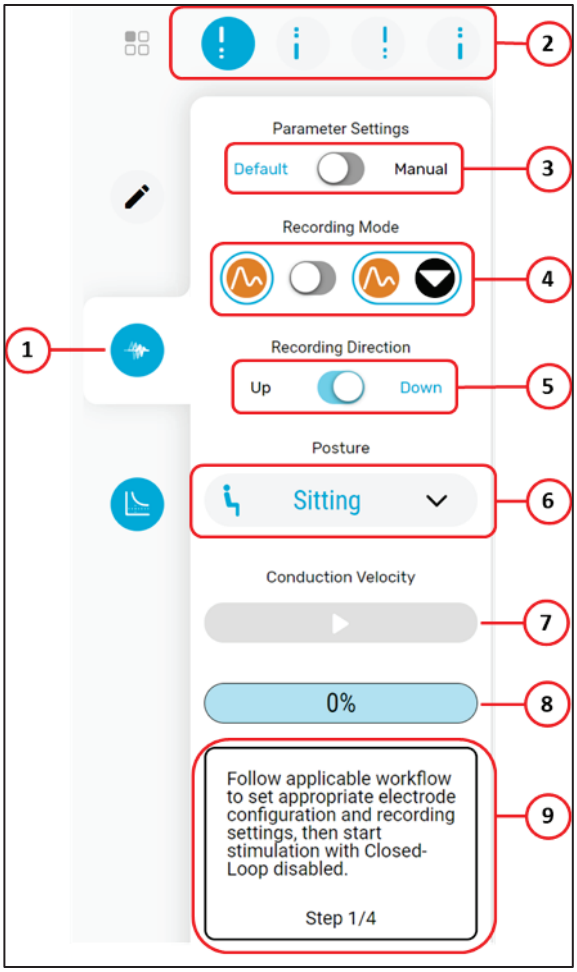


Figure 6.48: Layout of Neurophysiological Measurements Page (first tab).

1. Neurophysiological Measurements Page
2. Edit tab
3. Conduction Velocity (CV) tab
4. Chronaxie and Rheobase (CR) tab

6.5.2 Conduction velocity (CV) measurement

This is where you collect data to estimate the velocity at which elicited neural responses travel up or down the spinal cord. The CV measurement involves the CPA automatically moving the recording and (if applicable) reference electrodes at a fixed current level.



1. Conduction Velocity tab
2. Electrode Configuration options
    a. Stim at top of left lead
    b. Stim at bottom of left lead
    c. Stim at top of right lead
    d. Stim at bottom of right lead
3. Parameter Settings toggle
    a. Default(options above)
    b. Manual (settings made in Edit tab)
4. Recording Mode toggle
    a. Reference electrode (R-) is static
    b. R- moves w/ recording electrode.
5. Recording Direction toggle
    a. Up: recording electrode moves upward
    b. Down: recording electrode moves downward.
6. Posture drop-down
7. Start Measurement button
8. Measurement progress indicator
9. Workflow prompts

Figure 6.49: Layout of Conduction Velocity Tab.

To perform a conduction velocity measurement:

1. After completing Setup (Section 6.5.1).
2. Touch the Conduction Velocity tab.
3. Choose the Electrode Configuration option to use.

   If you want to use an electrode configuration that is different from the default options provided, set the Parameter Settings toggle to Manual, and configure the electrodes via the Manual tab.
4. Select the Recording Mode to use.

   - *Fixed Reference* for recording configurations in which the reference electrode is to remain fixed (only the recording electrode will be automatically moved).
   - *Fixed Distance* for recording configurations in which the reference electrode is to remain a fixed distance from the measurement electrode (recording and reference will be automatically moved together).

5. Adjust the initial measurement electrode positions if needed.
    - The recording electrode is usually placed near the stimulation electrodes (with a gap of at least 1 blank electrode).

    ⚠ **Caution**: To avoid patient discomfort do NOT place the recording electrode directly adjacent to any stimulation electrodes (stimulation or return).

    - For fixed reference recordings, the reference electrode is usually placed on the case electrode (E25), or on the end of the lead furthest from the stimulation electrodes.
    - For fixed distance recordings, the reference electrode is typically placed 2 or 3 electrodes from the measurement electrode.
6. Set the Recording Direction for the direction that the measurement electrode should move.
7. Select the Posture that the patient is in, so that this note will be collected with the measurement data.
8. The Workflow Prompts will guide you through what to do next. Light blue highlights will indicate which button(s) the system is anticipating you to touch next.

    For example, if the C- button is highlighted 

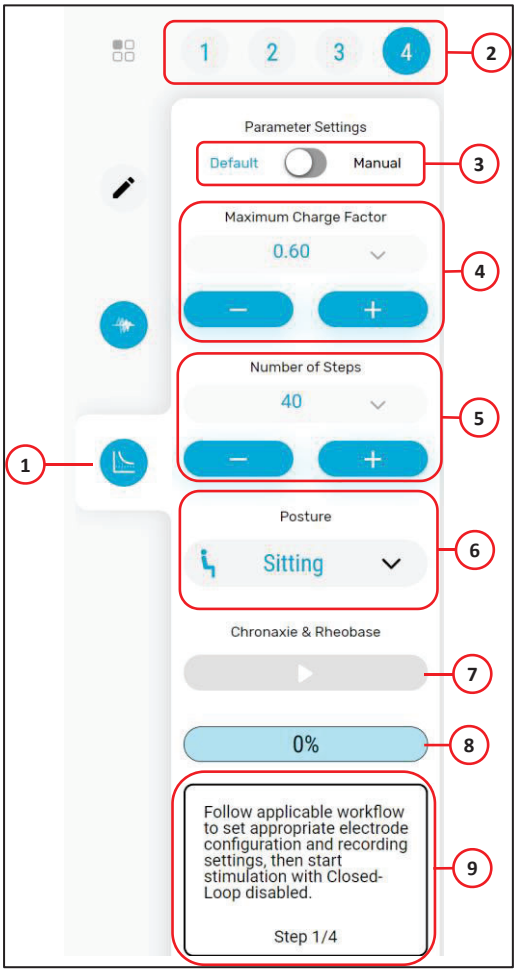
, the workflow will proceed the next step when you have clicked the C- button.
9. Start stimulation with closed-loop disabled.
10. Ask the patient to remain still for the duration of the test, then increase the current until the patient reports that it is at a strong comfortable level, and touch the C- button.
11. Touch the **Start Measurement** button  to begin data collection.
    - The **Start Measurement** button will be replaced with a **Stop Measurement** button  .
    - Touch the **Stop Measurement** button at any time to end the measurement.
12. When the measurement is complete (or when it has been stopped), current will ramp down and off automatically.
13. To collect more measurements (e.g. with different configurations), return to Step 3 in this section.
14. After completion of the measurements, return to the Programming (P) page.

    The stimulation settings of each program will return to the state they were in before you entered the Neurophysiological Measurements (P+) page.
15. Start stimulation on any of the restored programs that have a sync icon to save the them to the stimulator again.

    This will ensure that the programs on the stimulator are set back to their original.
16. Use the RECAP Viewer to calculate conduction velocity using the data that was collected. Refer to Evoke SCS System RECAP Viewer User Manual for instructions.

6.5.3 Chronaxie and Rheobase (CR) measurement

This is where you collect data to estimate the chronaxie and rheobase of the stimulated neurons. The CR measurement involves the system automatically increasing and decreasing current at different pulse widths. You may stop stimulation at any time with the Stop button STOP.



1. Chronaxie and Rheobase tab
2. Program selector
3. Parameter Settings toggle
    a) Default (standard CR options)
    b) Manual (changes made in Edit tab)
4. Maximum Charge Factor (MCF)—setting
5. Number of Steps—setting
6. Posture drop-down
7. Start Measurement button
8. Measurement progress indicator
9. Workflow prompts

Figure 6.50: Layout of Chronaxie & Rheobase tab.

To perform a chronaxie and rheobase measurement:

1. After completing Setup (see section 6.5.1).
2. Touch the Chronaxie and Rheobase tab.
3. Select the program number to use for the measurement. Only S1 will be used.
4. If you need to make modifications to the program settings:
    a. Set the Parameter Settings toggle to Manual.
    b. Touch the Edit tab.
    c. Make changes to electrode configuration and stim parameters as needed, as you

would in the Programming page. The PW used here will be the initial PW used for the CR measurement algorithm.
Note: The pulse width must be greater than 240µs.

d. Return to the Chronaxie and Rheobase tab.

5. Adjust the maximum charge factor if needed (default is 0.60). A higher chart factor will cause current to increase less when the PW is decreased throughout the measurements.
6. Adjust the Number of Steps to alter how quickly the measurement will take. Default is 40 steps. A lower Number of Steps will allow for faster measurements, but with fewer data points.
7. The Workflow Prompts will guide you through what to do next. Light blue highlights will indicate which button(s) the system is anticipating you to touch next.

   For example, if the C- button is highlighted 

, the workflow will proceed the next step when you have clicked the C- button.
8. Start stimulation with closed-loop disabled.
9. Ask the patient to remain still for the duration of the test and to inform you if the stimulation becomes too strong. Inform the patient that the stimulation current and pulse width will be automatically adjusted by the CPA during the measurement.
10. With the patient ready to begin, increase the current until the patient reports that it is at a strong comfortable level, and touch the C- button.
11. Touch the **Start Measurement** button  to begin data collection.
    The **Start Measurement** button will be replaced with:
    Stop and **Pause** buttons  .

    a. Touch the **Pause** button, at any time, to stop the current from changing.
    This may be required if the patient does not want the stimulation to increase any further.
    The **Stop** and **Pause** buttons will then be replaced with:
    Resume and **Next** buttons  .
    The current will remain constant until you press one of those buttons.

    - Touch the **Resume** button to continue changing current in the same direction.
    - If current was increasing, touch the **Next** button to start the current decreasing (only do this if current was increasing). If you touch this button when current had already been decreasing, current will resume decreasing, and the measurement workflow will stop.

    b. Touch the **Stop** button to turn stimulation off and stop the chronaxie and rheobase measurement.
12. After completion of the measurement, return to the Programming (P) page.

    The stimulation settings of each program will return to the state they were in before you entered the Neurophysiological Measurements (P+) page.

13. Start stimulation on any of the programs marked as being out-of-sync.
    This will ensure that the programs on the stimulator are set back to their original
14. Use the RECAP Viewer to calculate chronaxie and rheobase using the data that was collected. Refer to Evoke SCS System RECAP Viewer User Manual for instructions.



6.6 Disconnect Page

The Disconnect page is where you review your programming session, view any changes made, and confirm final program settings prior to disconnecting from the stimulator. Please refer to Section 6.4.3.1 for additional program color descriptions and Section 6.4.3.6 for additional Stim-Set color descriptions.

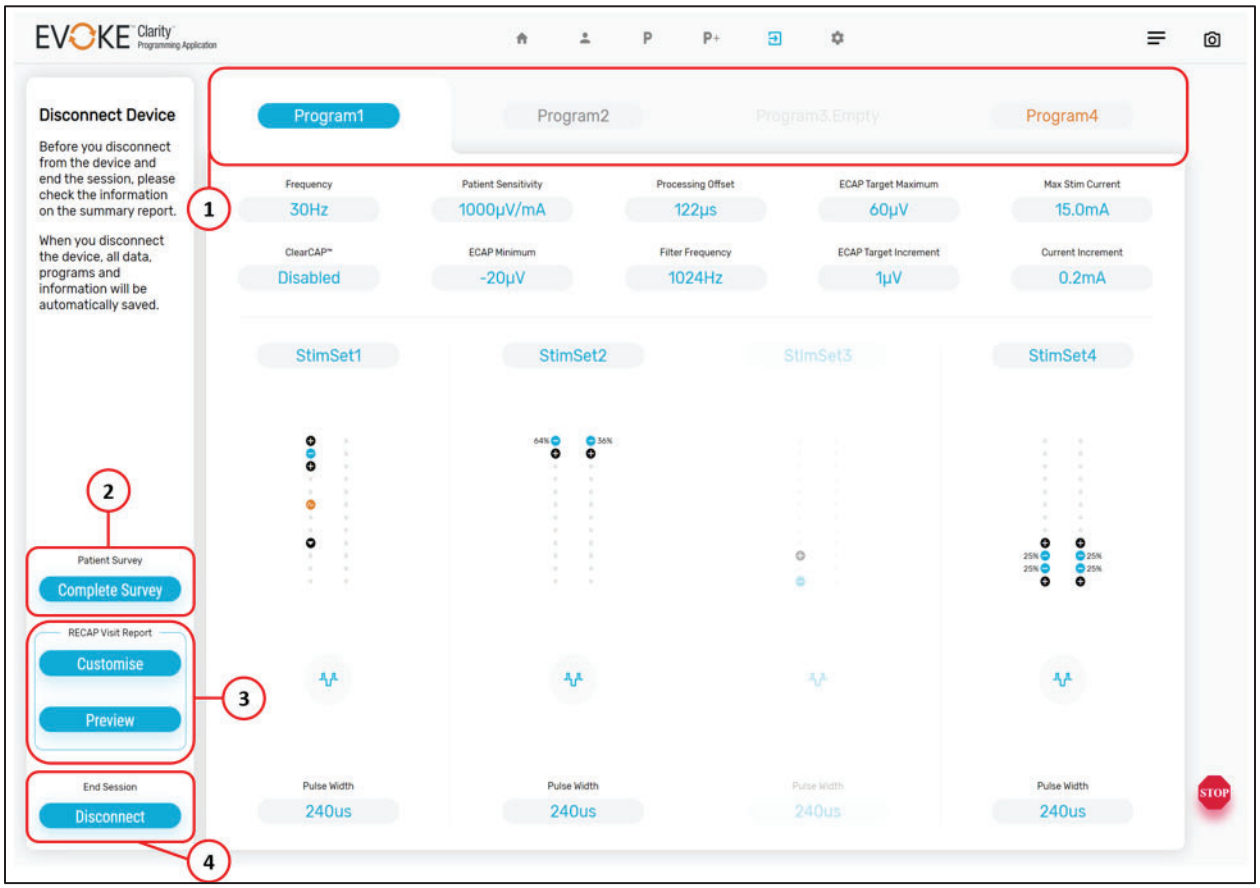


Figure 6.51: Disconnect Page Layout.

1. Final Programs
2. Patient Survey
3. RECAP Visit Report
4. End Session

Within the Disconnect page, there are three options to navigate to:

Patient Survey

1. Touch 'Complete Survey' if a survey was not already completed during the session. This will navigate you back to the *Patient* Page. Refer to Section 6.3.3 for more information.

RECAP Visit Report

2. Select 'Customize' to select the parameters to display in the final RECAP Report.
3. Select 'Preview' to generate the RECAP Report with default settings.

End Session

4. Select 'Disconnect' to disconnect from the device. Upon disconnection the programs on the CPA will automatically be saved to the corresponding visit folder on the CI and the session will be ended.

6.6.1 Customize RECAP Visit Report

Within the RECAP Report, you can customize the information that is shown on the RECAP Visit Report. Towards the left center of the screen, the sections of the RECAP Visit report are listed out. These sections are nominally set to the default.

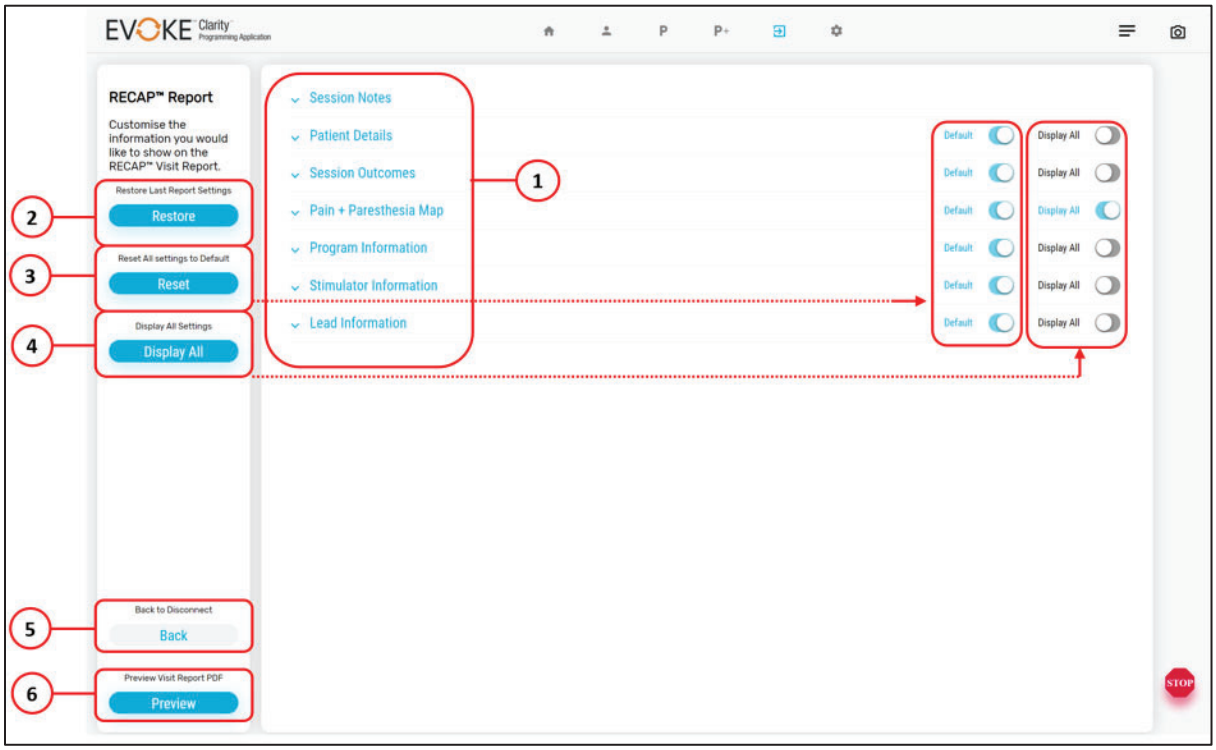


Figure 6.52: Customize RECAP Report Page Layout.

1. RECAP Report Sections
4. Display All settings

2. Restore Last Report Settings
3. Reset All settings to Default Visit
5. Back to Disconnect
6. Preview Visit Report PDF

Expanding and Selecting RECAP Visit Report Items

1. To see the entire list of what is in each section, select the carot ˅ or ^ next to the header to expand or collapse.



Figure 6.53: Expanding/Collapsing RECAP Visit Report Sections.

2. The user can then customize the report to:
    a. Show the Default settings
    b. Display all settings,
    c. Restore last report settings
    d. Manually choose what is in the report.

3. Once you finish customizing the report, touch the 'Preview' button to generate the report.

6.6.2 Preview RECAP Visit Report

Verify that the RECAP Visit report is acceptable per the Clinician's Requirements. The RECAP Visit Report is generated from the programming changes (comparing the first connection in a day to the settings when the report is generated) and the latest patient survey that was filled out for the current visit date.

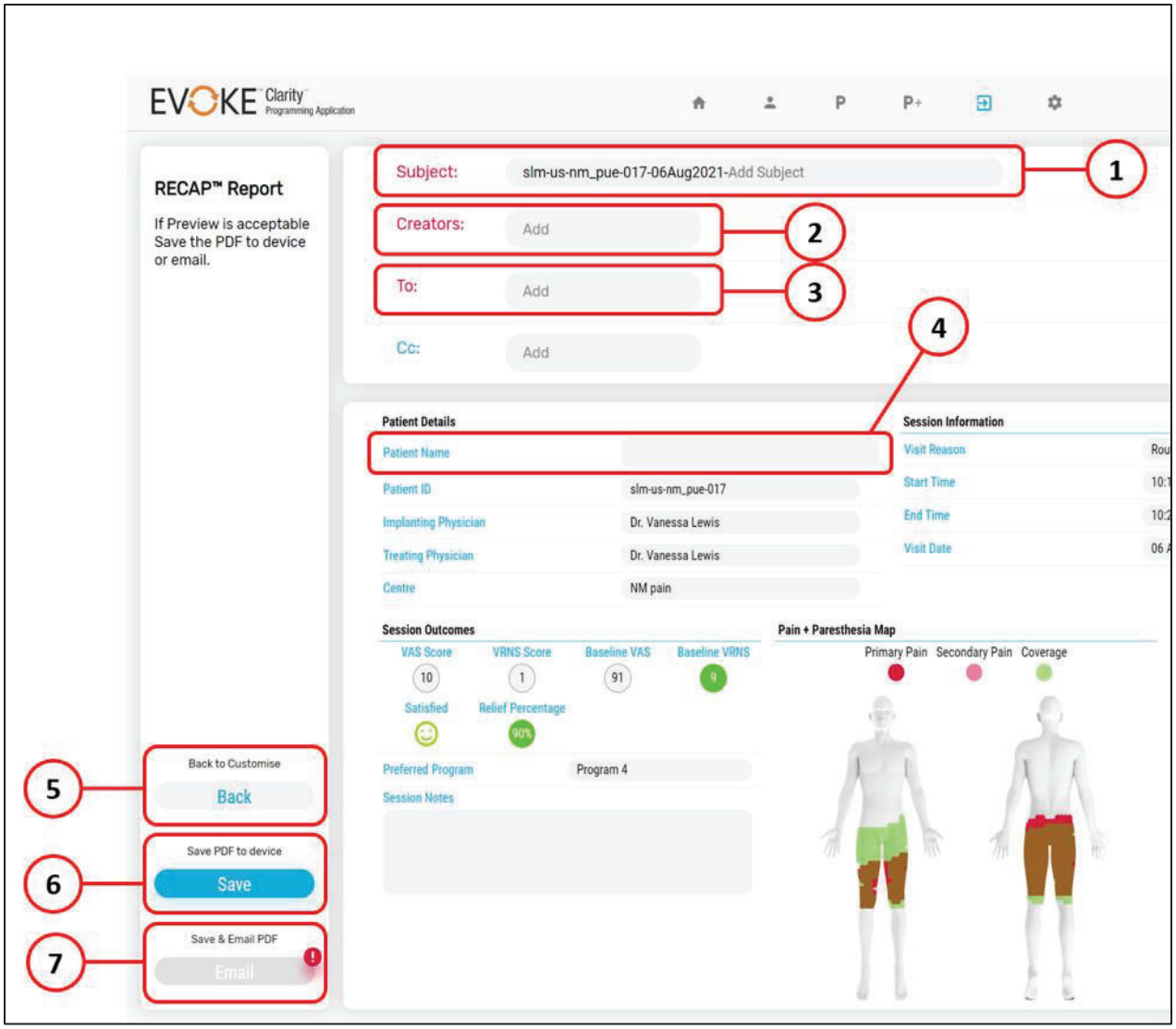


Figure 6.54: Preview RECAP Report Page Layout.

1. Subject: Add 'Email Subject'
2. Creators: Add 'Email address'
3. To: Add Recipient's 'Email address'
4. Add Patient Name
5. Back to Customize
6. Save PDF to device
7. Save & Email PDF

There are two options to select from: 'Save PDF to device' or 'Save & Email PDF'.

Save PDF to device

1. Touch 'Save'. The RECAP Visit Report will be saved to the CI as a PDF in the 'SaveFiles' folder (without any text in the 'Patient Name' field), for the corresponding Visit, and will automatically open in the installed PDF reader to ensure it looks as expected.

Save and Email PDF

1. If you plan to directly email the RECAP Visit Report to the clinician, fill out the

following sections (located at the top of the screen):

a. **Subject**: e.g. 'RECAP Visit Report'.

b. **Creators**: Email address of who is creating the report.

c. **To**: Intended recipient(s).

* If these sections are blank or not properly filled out, the section's label font will be **red** and there will be an  over the 'Email' button.

2. All sections' label font will be blue and the 'Email' button will also turn blue once the file is ready to be emailed.
3. Touch 'Email'.
    a. The RECAP Visit Report will be saved to the CI as a PDF in the 'SaveFiles' folder (without any text in the 'Patient Name' field), for the corresponding Visit, and will automatically open in the installed PDF reader.
    b. You will get a notification that 'The RECAP report will be emailed with next upload!'.

    Note: The report 'Creator' will also be emailed a copy of the report.
4. Once you disconnect and exit the CPA, this report will be located within the 'SaveFiles' folder of the visit (see Section 6.6.3).

6.6.3 Navigating to RECAP Visit Report

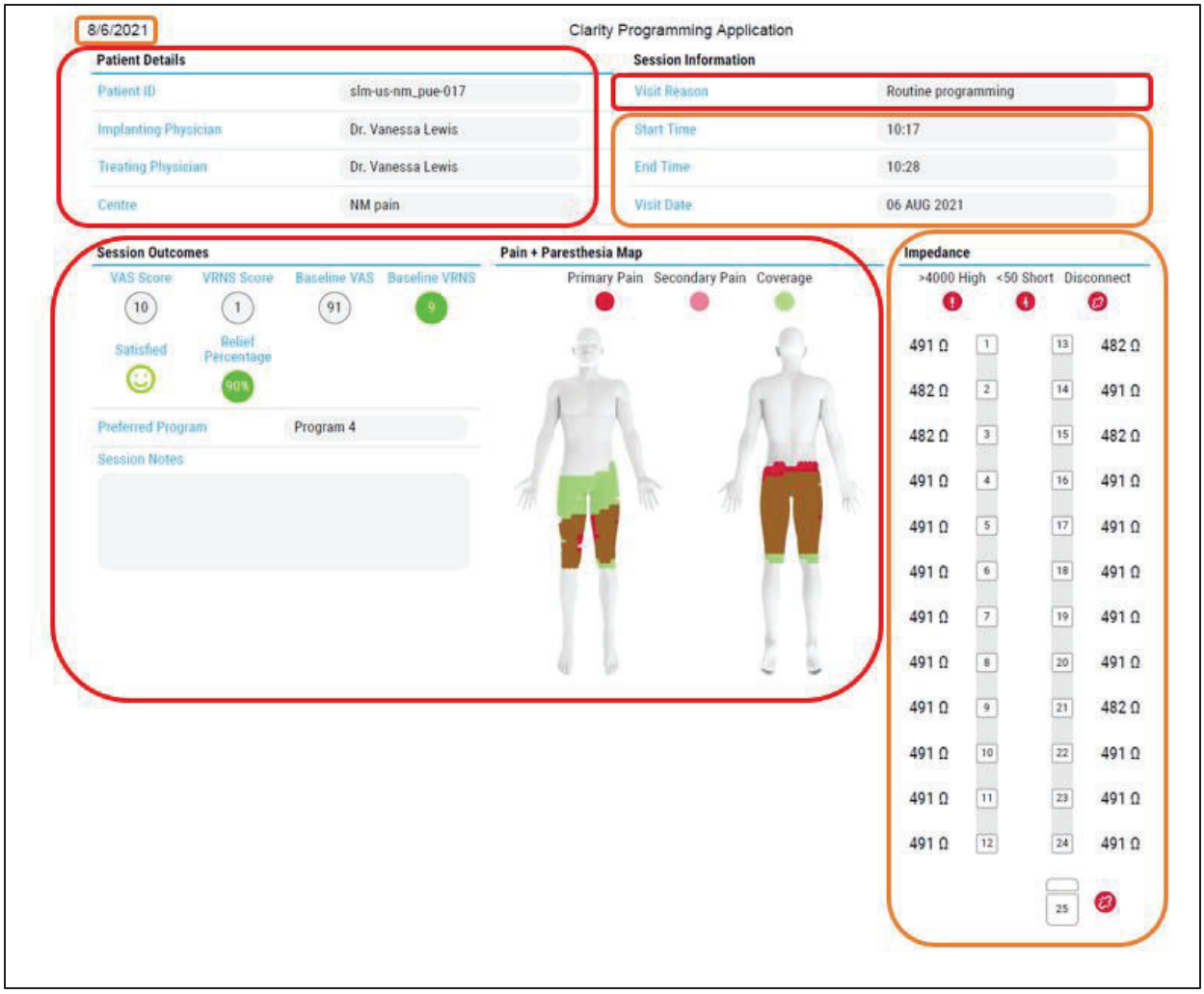
Saved RECAP Visit reports are saved in the same folder as SaveFiles. See Section 6.7.1.1 for instructions on where these folders are located on the C: drive.

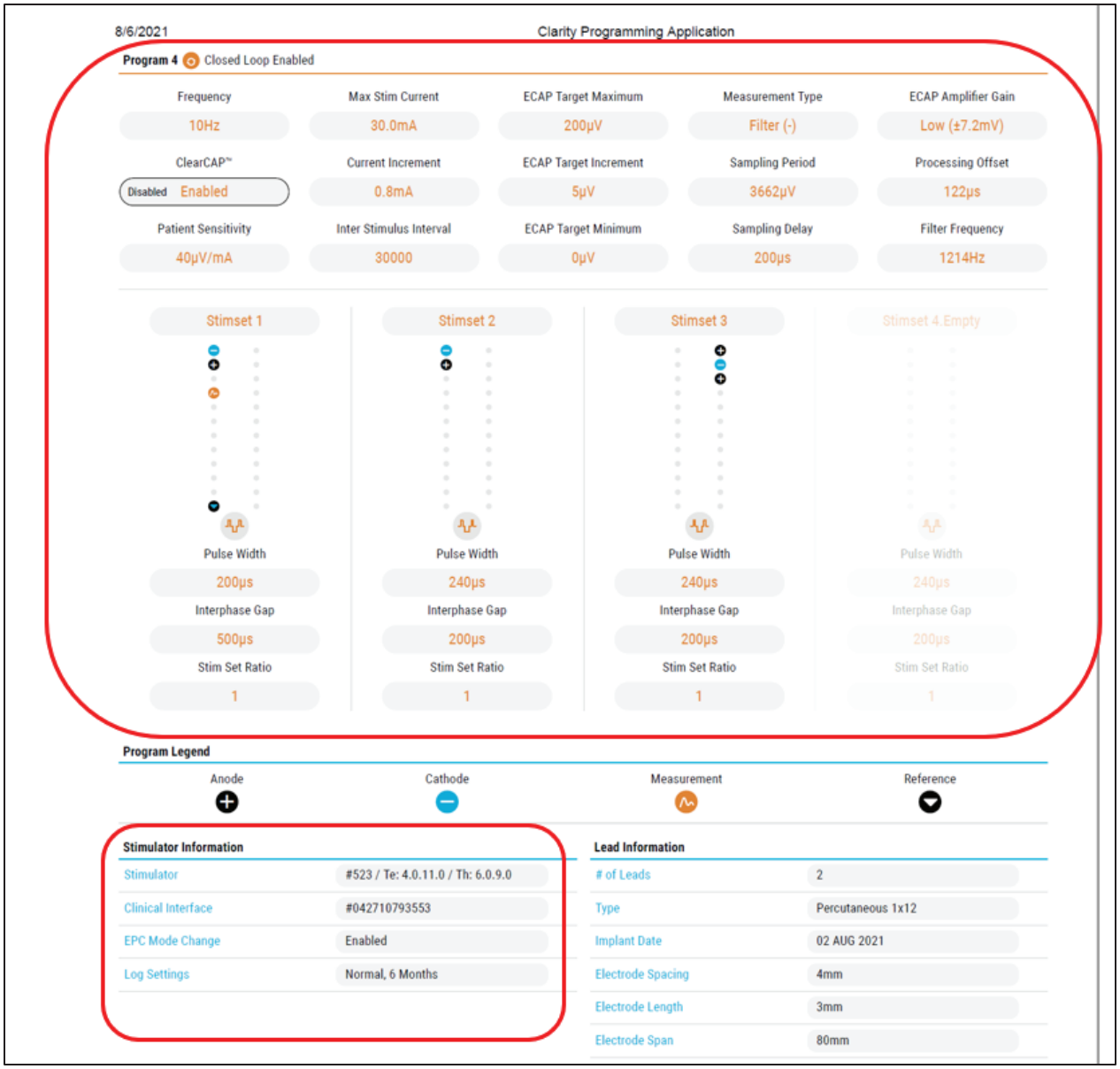
6.6.4 RECAP Visit Report

Below is an example of a RECAP Visit Report that 'displays all' information. Red boxes represent data that is obtained from this session's programming survey. Orange boxes represent data from the actual programming session and any changes that were made.

Additional Notes:

- Impedance – If impedance values are measured multiple times, the last measurement will be shown in the report.
- Programs – RECAP Visit Report will only show programs that are not empty.
- Program legend and Lead Information will be the same for every device.
- ClearCAP is represented by the change to the reference electrode  .


8/6/2021
Clarity Programming Application
Patient Details
Patient ID
slm-us-nm_pue-017
Implanting Physician
Dr. Vanessa Lewis
Treating Physician
Dr. Vanessa Lewis
Centre
NM pain
Session Information
Visit Reason
Routine programming
Start Time
10:17
End Time
10:28
Visit Date
06 AUG 2021
Session Outcomes
VAS Score
VRNS Score
Baseline VAS
Baseline VRNS
10
1
91
9
Satisfied
Relief Percentage
90%
Preferred Program
Program 4
Session Notes
Pain + Paresthesia Map
Primary Pain
Secondary Pain
Coverage
Impedance
>4000 High
<50 Short
Disconnect
491 Ω
482 Ω
482 Ω
491 Ω
482 Ω
491 Ω
491 Ω
491 Ω
491 Ω
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491 Ω
491 Ω
491 Ω
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8/6/2021
Clarity Programming Application
Program 4
Closed Loop Enabled
Frequency
10Hz
Max Stim Current
30.0mA
ECAP Target Maximum
200µV
Measurement Type
Filter (-)
ECAP Amplifier Gain
Low (±7.2mV)
ClearCAP™
Disabled
Enabled
Current Increment
0.8mA
ECAP Target Increment
5µV
Sampling Period
3662µV
Processing Offset
122µs
Patient Sensitivity
40µV/mA
Inter Stimulus Interval
30000
ECAP Target Minimum
0µV
Sampling Delay
200µs
Filter Frequency
1214Hz
Stimset 1
Stimset 2
Stimset 3
Stimset 4.Empty
Pulse Width
200µs
240µs
240µs
240µs
Interphase Gap
500µs
200µs
200µs
200µs
Stim Set Ratio
1
1
1
1
Program Legend
Anode
Cathode
Measurement
Reference
Stimulator Information
Stimulator
#523 / Te: 4.0.11.0 / Th: 6.0.9.0
Clinical Interface
#042710793553
EPC Mode Change
Enabled
Log Settings
Normal, 6 Months
Lead Information
of Leads
2
Type
Percutaneous 1x12
Implant Date
02 AUG 2021
Electrode Spacing
4mm
Electrode Length
3mm
Electrode Span
80mm

Programming parameter changed during programming session

- If no changes were made to a particular parameter during the programming session, the parameter will be listed as seen on the left-hand figure. The final setting will be centered in the appropriate colored font. Orange = Closed-loop Enabled or Blue = Closed-loop disabled.
- If a change was made to a particular parameter during the programming session (compared to programs on the stimulator on the first connection for that day), the original setting will be listed in black on the left and the entire parameter will be outlined in black.



Examples of Stim-Sets in RECAP Report



1. Stim-Set 1 – Enabled, electrode configuration changed during programming session. Small colored dots represent initial electrode configuration and large colored dots represent final electrode configuration
2. Stim-Set 2 – Disabled, empty since initial interrogation
3. Stim-Set 3 – Disabled, Stim-Set was erased during program session
4. Stim-Set 4 – Enabled, no changes made during program session



6.7 Settings Page

Touch the  to navigate to the *Settings Page*. On this page you will find the following information and buttons.

Application Version	CPA Firmware Version
Device ID	CI Serial Number
Language	English
Data Synchronization	Uploads files from the "SaludaData" folder on the CI to a centralized file server
CLS	External Closed-Loop Stimulator or Closed-Loop stimulator serial number, therapy and telemetry firmware versions
Log Setup	Set up therapy log settings: Size: Normal (1.5 MB) or Research (13 MB) Duration: 1 day to 1 year, Off
Software Reset button	Reset stimulator, clear Safe Mode errors, clear programs and reconnect
Factory Reset button	Restore devices to default factory settings. For use by Saluda Medical Field Clinical Engineer (FCE).
Enter Stock Mode button	Stop all CLS functions to conserve battery. Use the Charger to leave stock mode.
Exit CPA button	Exit the application.

6.7.1 Data Synchronization

6.7.1.1 *Data files*

All data downloaded from the stimulator and recorded during a programming session is saved to a clinical data log file (.log or .gz) on the CI, in a device folder, for later review. Folders are created and files are saved on the CI in the 'SaludaData' folder, per the following naming convention.

> This PC/Windows/ProgramData/ClarityData/SaludaData/<patient folder>/<visit folder>/

Where:

- An example of 'patient folder' is:
  20210721-2010-0089-8uc5-042120500000_SN0000 _
  Date of initial connection – unique identifier – CI serial number _ stimulator SN

- An example of 'visit folder' is: 2021-07-23.11-37-55.512
  Visit Date . Time of initial connection

For more information on the data files and how to view them, refer to the Evoke SCS System RECAP™ Viewer User Manual.

6.7.1.2 *Data upload*

The Data Synchronization feature within the CPA uploads files from the "SaludaData" folder on the CI to a centralized file server. Data upload can occur while connected to a patient and won't affect standard CPA functionality.

6.7.1.3 *Starting the data upload*

If enabled, the CPA automatically scans and attempts to upload new data every 30 minutes as long as the CI is connected to the internet. If connected to a stimulator, it will not attempt to upload the session currently in progress.

To manually start the sync:

1. Ensure the CI is connected to the internet.
2. Go to the System Settings page .
3. Touch the Start Sync 

button.

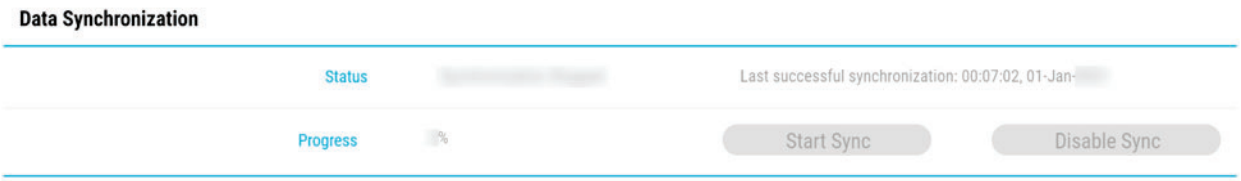


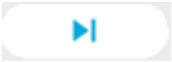
Figure 6.55: Layout of Data Synchronization section in System Settings page.

Button/Field	Description
Status	Can be any of the following: • **Synchronizing…** : Synchronization is in progress • **Connection Error**: No internet connection • **Invalid CI**: CI serial number is not approved • **Synchronizing Disabled**: Synchronization has been disabled • **Synchronizing Failed**: Synchronization failed to complete • **Synchronizing Complete**: Synchronization has completed successfully The Status also notes the date of last successful synchronization.

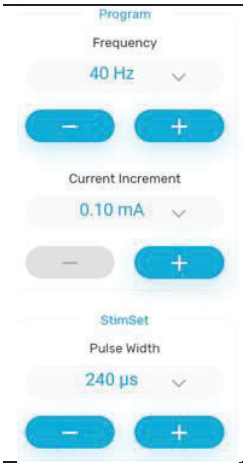
Progress	Indicates what percent of data has been checked and uploaded.
Start Sync button	Enables data upload to the server, running every 30 minutes. Will be available when not connected to a device and if synchronization is currently disabled. Will be disabled when you start synchronization. **Note:** You cannot manually enable synchronization while connected to a device (however, if it is already enabled it will upload all but the current session in the background).
Disable Sync button	Prevents data synchronization until it is re-enabled. Will be available if synchronization is currently enabled.

7. CPA – Settings guide

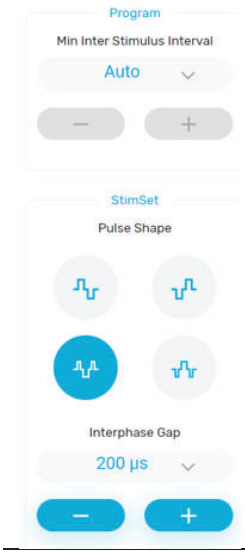
7.1 General CPA buttons and icons

	Add Button (if standalone)		Increase Button
	Alert Icon – toggle over icon to see error details		Increase Stimulation Button
	Clear Pain Drawing Button		Load Button
	Collapse Button		Next Button
	Decrease Button		Paint Button
	Decrease Stimulation Button		Pause Button
	Delete Button		Save Button
	Download Button		Save Program Button
	Edit Button		Start button
	Erase Button		Stop Button
	Expand Button		Stop Stimulation Button
	Exit/Close Button		Sync Icon
			Toggle Button

7.2 Coverage Settings



Basic	
Frequency (Hz) *	10 – 1400 Hz closed-loop disabled 10 – 250 Hz closed-loop enabled
Current Increment*	0.05 mA – 4.0 mA (depending on the electrode setup)
Pulse Width^	20 – 1000 µs



Advanced	
Min Inter-Stimulus Interval*	Interval of Stim-Set pulses Auto (minimum permitted ISI), 1400 – 50000 µs
Pulse Shape^	Biphasic - Positive first, Negative first Triphasic - Positive first, Negative first
Interphase Gap^	20 – 500 µs

Note: *Stim-Set Parameters^* only apply to the selected Stim-Set. *Program Parameters* * apply to all Stim-Sets. The available range of each setting is shown.

7.3 Acquisition Settings

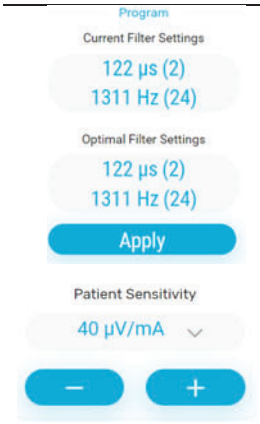


Basic	
Sampling Period*	122 – 10009 µs (2 – 164 samples)

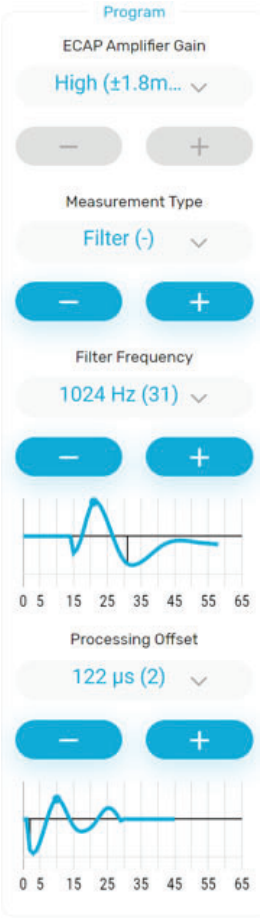
Advanced	
ECAP Amplifier Gain*	Evoked Compound Action Potential telemetry amplifier gain setting. High (± 1.8 mV), Low (± 7.2 mV), Disabled
Sampling Delay*	100 – 1000 µs
ClearCAP*	Disable or Enable ClearCAP stimulation. Sets the Reference electrode as an input for ClearCAP.
MES Active^	*Disable* or *Enable* the measurement electrode scan for the duration of the programming session.
MES Options	Measurement electrode scan position configuration options. Optimal, Fixed Reference, Fixed Measurement, Fixed Distance.

Note: *Stim-Set Parameters^* only apply to the selected Stim-Set. *Program Parameters* * apply to all Stim-Sets. The available range of each setting is shown.

7.4 Filter Settings



Basic	
Optimal Filter Settings*	Press *Apply* to use recommended filter sample
Patient Sensitivity*	14 – 1000 µV/mA

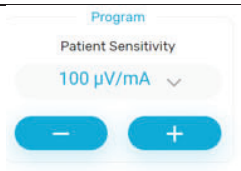


Advanced	
ECAP Amplifier Gain*	Evoked Compound Action Potential Telemetry amplifier gain setting. High (± 1.8 mV), Low (± 7.2 mV), Disabled
Measurement Type *+	ECAP Sampling Disabled, Filter (+), Filter (-), Amplitude **Note:** For Raw data, Closed-loop is disabled and the settings for Processing Offset, Processing Period, Patient Sensitivity, and ECAP Target Increment are disabled.
Filter Frequency * (Filter +/- mode only)	496 – 1928 Hz (65 – 16 samples)
Filter Frequency plot (Filter +/- mode only)	ECAP amplitude vs. filter samples. Circle – recommended samples (peak of plot) Black line – samples used.
Processing Offset*	0 – 3662 µs (0 – 60 samples)
Processing Offset plot	ECAP amplitude vs. processing offset. Circle – recommended offset (peak of plot); Black line – offset used.

Note: *Stim-Set Parameters*^ only apply to the selected Stim-Set. *Program Parameters* * apply to all Stim-Sets. The available range of each setting is shown.

+ For measurement, stimulation frequency must be 250 Hz or less for Raw Data and Amplitude, or 200 Hz or less for Filter (+/-) or if ClearCAP is enabled.

7.5 Evaluation Settings

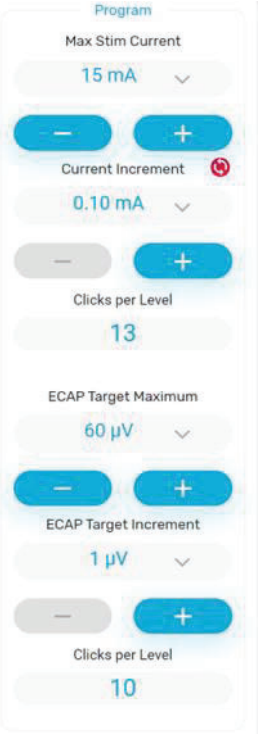


Basic	
Patient Sensitivity*	14 – 1000 µV/mA

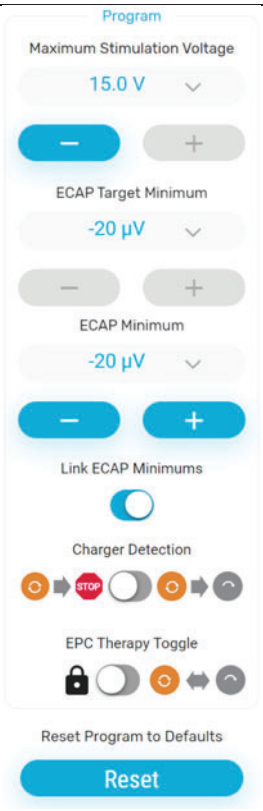
Note*: Program Parameters* * apply to the selected program. The available range of each setting is shown.

7.6 Program Settings

Program Settings apply to the selected program. The available range of each setting is shown.



Basic	
Maximum stimulation current	1 – 50 mA
Current Increment	0.05 mA – 4.0 mA (depending on the electrode setup and Max Stim Current)
Clicks per level (CL disabled)	Calculated number of clicks to change 1 light on the EPC to the next (depending on Max Stim Current and Current Increment)
ECAP Target Maximum	-900 – 10000 µV
ECAP Target increment	1 – 1000 µV
Clicks per level (CL enabled)	Calculated number of clicks to change 1 light on the EPC to the next (depending on ECAP Target Max and ECAP Target Increment)
Advanced	
Max Stimulation Voltage	7.5 – 15 V
ECAP Target Minimum	Minimum ECAP Target that can be set with the CPA or EPC (-1000 – 1000 µV)
ECAP Minimum	Minimum ECAP amplitude recorded by the stimulator (-1000 – 1000 µV)



Link ECAP Minimums Toggle	Link 'ECAP Target Minimum' to the 'ECAP Minimum' value (enabled, default) or not linked (disabled).
Charger Detection Toggle	Charger detection disables Closed-Loop enabled programs during CLS charging. When charging is started with stimulation on, if the mitigation is: • Enabled , stimulation continues, with CL disabled. • Disabled (default), then if: ○ **CL enabled**: stimulation stops. ○ **CL disabled**: Stimulation continues. **Note:** This needs to be set for each program.
EPC Therapy Toggle	When EPC Therapy is *Enabled* , CL can be enabled/disabled from the EPC. When EPC Therapy is *Disabled* (default), CL cannot be enabled/disabled from the EPC. **Note:** This is a global setting and applies to all programs.
Reset Program to Defaults	Reset the selected program to default parameters and delete all but the first Stim-Set (S1).

7.7 Program Management Settings

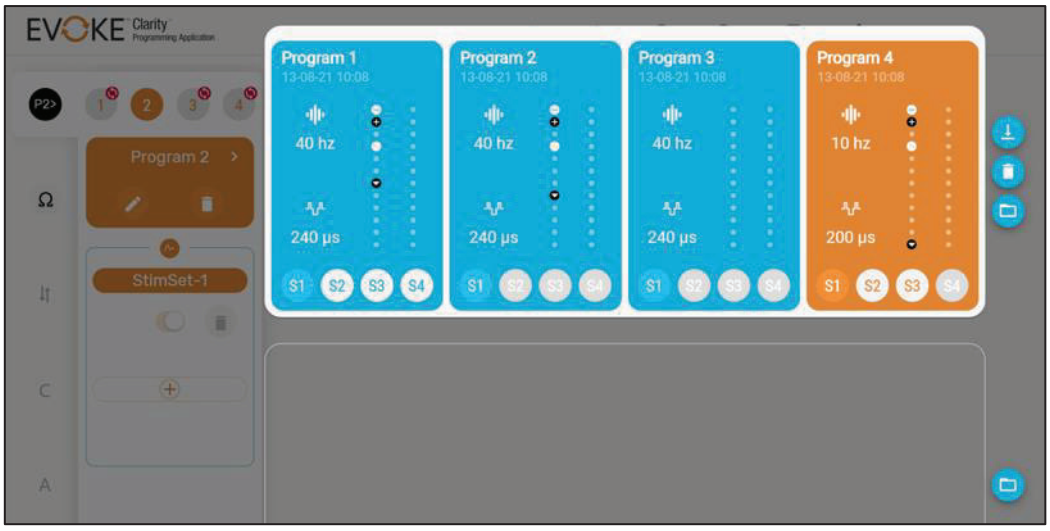


Figure 7.1: Program Management Settings.

Program Selection	Program, labeled Program 1 (P1), Program 2 (P2), Program 3 (P3), Program 4 (P4)
Stim-Set Selection	Stim-Set slots, labeled Stim-Set-1 (S1), Stim-Set-2 (S2), Stim-Set-3 (S3) or Stim-Set-4 (S4). Dark grey circles with white font represent non-enabled Stim-Sets.
Save Slot	Holds information from all 4 programs, as displayed on the CPA at the time they were saved. Automatically occurs upon connection to a stimulator
Red Sync Icon	Represents an Unsynchronized program Located next to the number of the program Any program on the CPA that has not been run on the stimulator • New program • Modified program

8. Behavior of the stimulator when alerts occur

Refer to Section 6.1.2 for how notifications are displayed on the CPA.

8.1 Out of Compliance

Out of Compliance (OOC) occurs when the voltage requirement exceeds the Maximum Stimulation Voltage (see Section 7.6). This may also occur with disconnected stimulation electrodes. When OOC is indicated, the patient may not increase intensity with the EPC, stimulation may stop, or the patient may feel a reduction in paresthesia intensity.

If OOC occurs with disconnected stimulation electrodes, or recording electrodes with ClearCAP enabled, then stimulation stops. If the electrodes are reconnected (e.g. their impedance reduces), stimulation may be restarted by the patient using the EPC and will ramp from 0 mA to the stimulation current set when the stimulator stopped. If the electrodes remain disconnected the stimulator will follow the behavior described in Section 11.3.

If OOC occurs when Closed-loop is enabled with electrodes connected, and the stimulator does not detect a problem with the ECAP measurement, then the stimulator will reduce the target value by half. If the stimulator detects a potential problem with the ECAP measurement, then stimulation stops. When stimulation is restarted by the patient, it will start at 0 mA of stimulation current, with Closed-loop disabled, and the patient will need to increase the stimulation intensity using the EPC. Closed-loop is automatically re-enabled, without interrupting stimulation, once the ECAP signal is detected. The system determines an ECAP has been detected when the ECAP amplitude reaches half the original target value.

If OOC occurs when Closed-loop is disabled with electrodes connected then stimulation will continue.

8.2 Reference Clock Error

A reference clock error is an indication that the timing used to generate the stimulation pulse is incorrect. When a reference clock error is indicated, Closed-loop is disabled until the error is cleared. Stimulation stops if the error is detected during multiple consecutive stimuli.

8.3 Electrode Disconnected

When the clinician or patient attempts to start stimulation, the stimulator checks the connection of each stimulation and recording electrode (if selected). If one or more stimulation electrodes are disconnected, then stimulation will not start. If one or more recording electrodes are disconnected, then stimulation will start with Closed-loop disabled.

8.4 Current at Maximum

If the stimulation current is at its maximum setting when Closed-loop is enabled, stimulation may stop, the patient may feel a reduction in paresthesia intensity, or Closed-loop may be disabled. If

recording electrodes are disconnected, then stimulation stops. When Closed-loop is enabled, if the stimulator detects a potential problem with the ECAP measurement, then stimulation stops, and Closed-loop is disabled until the ECAP measurement returns, as described in Section 8.3.

If the stimulator does not detect a problem with the ECAP measurement when Closed-loop is enabled, then the stimulator will reduce the target value by half. If the stimulator detects a potential problem with the ECAP measurement, then stimulation stops. When stimulation is restarted, it will start at 0 mA of stimulation current, with Closed-loop disabled, and the patient will need to increase the stimulation intensity using the EPC. Closed-loop is automatically re-enabled, without interrupting stimulation, once the ECAP signal is detected. The system determines an ECAP has been detected when the ECAP amplitude reaches half the original target value.

8.5 Clipping

For each stimulus, the stimulator checks the ECAP signal is within the ECAP amplifier gain limits. If the ECAP signal is outside these limits, or clipping, the stimulator checks the connection of each recording electrode. Stimulation may stop, the patient may feel a reduction in paresthesia intensity, or Closed-loop will be disabled until the clipping alert is cleared.

If Closed-loop is enabled and clipping occurs with disconnected recording electrodes, then stimulation stops. If the recording electrodes are reconnected, stimulation may be restarted by the patient using the EPC and will ramp to the target level set when the stimulator stopped. If the recording electrode remains disconnected the stimulator will follow the behavior described in Section 11.3.

If Closed-loop is enabled and clipping occurs with the recording electrodes connected, the stimulator will set the ECAP amplifier gain to Low and stimulation will continue. If clipping continues and the gain is already Low, the stimulator will reduce the target value by half and stop stimulation. When stimulation is restarted, it will start at 0 mA of stimulation current, with Closed-loop disabled, and the patient will need to increase the stimulation intensity using the EPC. Closed-loop is automatically re-enabled, without interrupting stimulation, once the ECAP signal is detected. The system determines an ECAP has been detected when the ECAP amplitude reaches half the original target value.

If Closed-loop is disabled and clipping occurs with disconnected recording electrodes while ClearCAP is enabled, then stimulation stops. If the recording electrodes are reconnected, stimulation may be restarted by the patient using the EPC and will ramp to the stimulation current level set when the stimulator stopped. If the recording electrode remains disconnected the stimulator will follow the behavior described in Section 11.3.

If Closed-loop is disabled and clipping occurs with disconnected recording electrodes while ClearCAP is disabled, then stimulation continues.

If Closed-loop is disabled and clipping occurs with the recording electrodes connected, the stimulator will set the ECAP amplifier gain to Low and stimulation continues.

9. Evoke Charger

Refer to the Evoke SCS System User Manual for full details on use of the Evoke Charger to charge the CLS.

The stimulator battery status is displayed in the status bar (see Section 6.2.3). If the stimulator is being charged when connected to the CPA, an indication is displayed on the stimulator battery icon.

9.1 Stimulation during charging

9.1.1 Closed-loop disabled

When closed-loop is disabled, charging does not affect stimulation.

Note: During charging, ECAP measurements may be distorted by the charging field.

9.1.2 Closed-loop enabled

When closed-loop is enabled:

1. Stimulation should be stopped before charging is started. Stimulation can be stopped using the CPA or the EPC (see Evoke SCS System User Manual).
2. During charging the CLS automatically disables closed-loop stimulation.
3. After charging has started, stimulation may be turned on, but closed-loop will remain disabled. Stimulation will restart at the current level saved when stimulation was stopped.
4. If charging starts while stimulation is on, the CLS can be set using CPA to respond in one of two ways (see Section 7.6):



(Default setting)

   a. Stimulation will **automatically stop** when charging is detected. After charging has started, stimulation may be turned on, but closed-loop will remain disabled. Stimulation current will be set to 0 mA and the patient can increase it with the EPC.



   b. Stimulation continues with **closed-loop disabled** when charging is detected, and the stimulation current is set to the minimum from the previous 10 seconds.

5. After charging has finished, the CLS will wait 25.25 seconds and then automatically enable Closed-loop. If stimulation is on, the ECAP amplitude target is set to the smaller of: the target before charging started; or the average ECAP amplitude from the 5 seconds before Closed-loop is automatically enabled.

⚠ **Caution**: Refer to the Evoke SCS System Surgical Guide for precautions when operating equipment. During charging, closed-loop is disabled, so patients should turn stimulation off if charging while driving or operating equipment.

Note: When the CLS automatically enables or disables closed-loop stimulation, the patient may feel changes in paresthesia intensity.

Note: During charging, ECAP measurements may be distorted by the charging field.

10. Patient education and ID card

Educate the patient on the use of their EPC and Charger (if applicable) using the Evoke SCS System User Manual.

All patients should be supplied with a Patient ID card for the clinician to complete.

1. Give the completed Patient ID card to the patient so that they can use it to show other medical practitioners or security personnel that they have an active implanted medical device.
2. Educate the patient to show the Patient ID card to healthcare professionals before undergoing any medical procedure.
3. The Patient ID Card indicates that the Evoke System is MR Conditional in certain system configurations, under specific scanning parameters. The card advises the patient to inform their physician if an MRI is being considered and to refer to the MRI clinical staff to the Evoke SCS System MRI Guidelines accessible at https://www.saludamedical.com/manuals.

11. Maintenance of the Evoke CI and Evoke CST

11.1 Maintenance of the Evoke CI

Maintenance and cleaning of the Clinical Interface should be carried out according to instructions in the device manual accompanying the CI tablet.

11.2 Updating the Evoke CI Software

The CI contains software that automatically checks if there are any updates that can be downloaded and applied to the CI. The CI must be connected to the internet for this check and update to be completed.

When the software detects that an update is required it will show the following message:

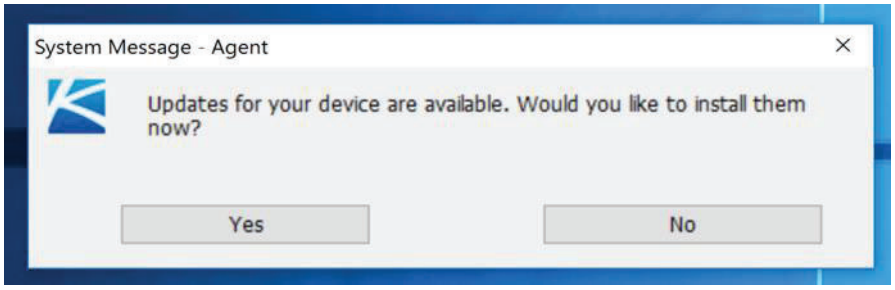


Figure 11.1: Prompt message for software update.

Touch “Yes” to download and apply the updates now, or “No” if you wish to update later.

> **Note:** The update should be applied as soon as possible, but if there is not sufficient time the software will continue to popup reminders until the update is applied.

The update process will take several minutes during which you will be unable to use the programs. You will receive a message once the update for each program is complete.

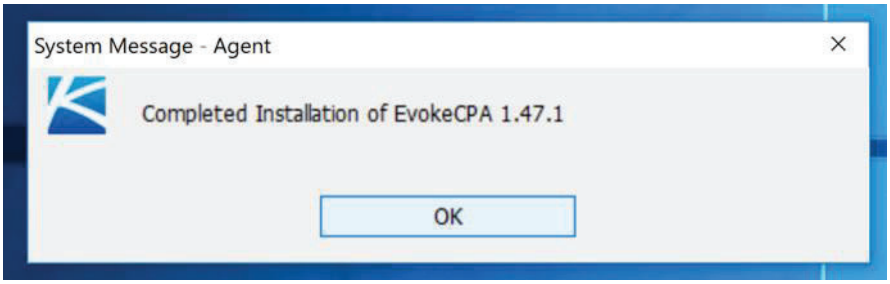


Figure 11.2: Example program update message.

You will receive another message once the full update process has been completed and the CI is ready for use.

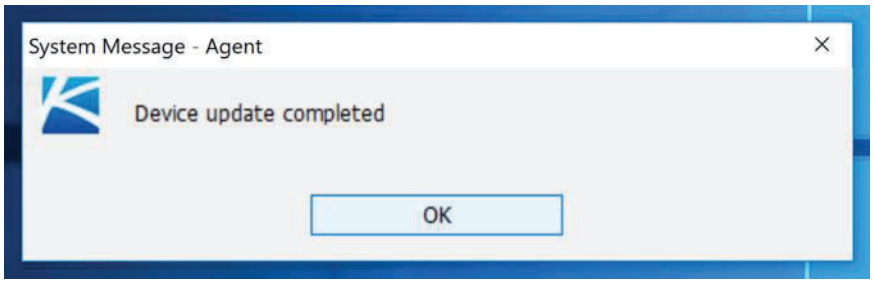


Figure 11.3: Device update completion message.

⚠ **Caution:** It is important to apply the updates as soon as possible as they may contain important safety or security improvements.

11.3 Maintenance of the Evoke CST

The CST is not expected to be in direct contact with patients but should still be periodically cleaned. The CST can be cleaned with a soft cloth dampened with a mild disinfectant or alcohol.

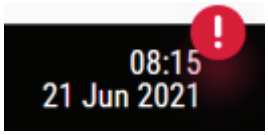
Refer to the Evoke SCS System User Manual for advice on the maintenance of additional components of the Evoke SCS System.

11.4 Disposal of devices

DO NOT dispose of the CI or the CST in municipal waste facilities. Please return any items to Saluda Medical via your Saluda Medical representative for proper disposal.

12. Troubleshooting

Table 12.1: Troubleshooting.

Issue	Likely Explanation(s)	Corrective Action(s)
CI will not turn on.	CI battery may need recharging.	Attach power supply to CI and plug into power outlet.
CI does not respond or is slow to respond	CI operating system may not be functioning correctly	Restart the CI by shutting down or restarting. If the CI does not respond, shut down the CI by pressing the power button for 10 seconds. Then release the power button and press it again to restart the CI.
Programming software (‘Clarity’) icon is not visible.	Icon may have been moved or deleted.	Using the CI search function, locate and select the 'Clarity'. The program should start. If this procedure fails, please call your Saluda Representative.
Touching the programming software (‘Evoke CPA’) icon does not start the software.	The shortcut link has been broken or target file moved.	Using the CI search function, locate and select ‘Clarity’. The program should start. If this procedure fails, please call your Saluda Representative.
Stimulator cannot be found by CPA.	Stimulator battery may need recharging or is in Stock Mode.	Apply the Charger to the stimulator, charge if required.
CST to stimulator connection fails due to time out.	CST may be too far from stimulator.	Move CST closer to stimulator. Ensure no EMI from other devices. Restart the CPA and/or the CI if issues persist.
Exclamation mark appears over CI time. 	Stimulator time is not synchronized.	Synchronize stimulator time (Section 6.2.2), confirm the exclamation mark disappears. **Note:** Stimulation must be off.
Unable to start stimulation on CPA.	Stimulation may already be running and the CPA is out of sync.	Press the ‘Stop’ button again to ensure stimulation is off.

Issue	Likely Explanation(s)	Corrective Action(s)
	Minimum electrode configuration has not been programmed.	Configure required electrodes (Section 6.4).
	Stimulation parameters may exceed allowable limits.	Check pulse width, frequency, current increment, maximum current, interphase gap (IPG), and sampling period and ensure the combination in use is within system limits.
Patient cannot feel increasing stimulation	Stimulation may not be at Threshold yet.	Continue to increase stimulation until patient reports feeling stimulation.
	Communication may be disrupted - Active Current level not changing while Current Setpoint continues to increase (Section 6.4.4.1).	Stop stimulation. Ensure there is good communication (Section 6.1.2.5), move CST closer to stimulator. Poor Communication  Good Communication  Ensure no EMI from other devices. Restart the CPA and/or the CI if issues persist.
Cannot enable Closed-Loop on CPA.	Recording electrodes have not been configured or are disconnected.	Check electrode impedances (Section 6.4.1). Configure recording electrodes (Section 6.4.4.2).
	Sampling period may be too small.	Increase sampling period/number of samples ('+' button).
Parameter or control button greyed-out.	Certain rules may not be met for the current program configuration.	Check for notification icons on certain buttons and the information in the *Notes* (Section 6.1.2).
	Parameter may not be adjustable in the current mode.	Turn stimulation off and attempt to adjust the parameter to the desired level.
No data in rolling plot or rolling plot lacks data points and appears 'lumpy' or ‘spiky’.	System may be busy or MES may be enabled.	Ensure MES is disabled. Wait for condition to clear or re-start software. Close other applications that are running (e.g. RECAP Viewer).
	Communication may be disrupted.	Move CST closer to device. Ensure no EMI from other devices (e.g. phone).

Issue	Likely Explanation(s)	Corrective Action(s)
CPA freezes or has very slow response.	Other applications open.	Restart the CPA. Close other applications that are running. Ensure the CST is close to the stimulator. Ensure no EMI from other devices (e.g. phone).
Patient cannot raise stimulation to their desired level using the EPC.	Maximum Stimulation Current may be too low.	Raise Max Stim Current (Section 7.6).
	ECAP Target Maximum may be too low.	Raise ECAP Target Maximum (Section 7.6).
Patient or Programming clinician cannot raise stimulation above zero with the EPC.	Stimulator may be in *Safe Mode*.	Perform 'Soft Reset' (Section 6.7).
	Stimulator may be reaching voltage compliance limit (Section 8.1). Stimulator may have Electrode Disconnected error (Section 8.3).	Perform an impedance check to ensure all connections are ok (Section 6.4.1). **If an eCLS:** Check intraoperative cable, lead adapter and eCLS connections.
	EPC may not be communicating with the stimulator.	Ensure you have disconnected with the CPA. Check that the audio indicators are enabled and if 3 beeps are heard bring the EPC closer to the stimulator and try again.
Patient reports high variability in stimulation.	Stimulator needs device check and possible reprogramming. Interrogate with the CI/CPA to confirm CL is enabled, noting any error messages.	Reprogram the stimulator and test new settings (Section 5). Check the Patient Sensitivity setting, remeasure the activation plot and ensure the ECAP signal is acceptable.
	Patient is moving while charging the CLS or eCLS	The CLS will only operate with CL disabled while it is being charged. Stimulation should be turned off or the patient should not move too much if the stimulation strength variation is unpleasant.

Issue	Likely Explanation(s)	Corrective Action(s)
Contact Clinician Indicator Light is on either Charger or EPC.	Stimulator is in *Safe Mode*. 	Note down the error on the screen; **Note:** You can take a screenshot with the CI by pressing and holding Fn+Windows+Spacebar. Perform 'Soft Reset' (Section 6.7).
CST not detected.	CST is not plugged in.	Plug CST into USB port and restart the CPA.
ClearCAP disabled error	Recording or reference electrode is disconnected.	Check electrode connectivity with an impedance check (Section 6.4.1).
Clipping causes stimulation to stop.	Recording or reference electrode is disconnected.	Check electrode connectivity with an impedance check (Section 6.4.1).
	Input to amplifier is too large.	Switch to low gain mode.
		Check the impedances and the connections to the stimulator if using an eCLS.
	Charging has been started while the stimulator is operating with CL enabled.	Restart stimulation, check the charger mitigation feature setting (Section 7.6).
Current at Maximum.	Maximum current limit may be too low.	If the patient does not report any surges in stimulation and only cutting out, increase the Max Stim Current (Section 7.6).
	High artifact.	Check the activation plot, if it is not the correct shape try changing recording or reference electrodes. Increase pulse width to reduce current requirement. Enable ClearCAP (Section 7.3)
	Electrode disconnection.	Check the impedances (Section 6.4.1) or refer to 'Electrode Disconnected' (Section 8.3).
	CL stimulation is on when charging is started.	Turn off the Charger and see if the problem persists; check the charger mitigation feature setting (Section 7.6).

Issue	Likely Explanation(s)	Corrective Action(s)
Out of Compliance.	Voltage limit may be too low.	Confirm voltage limit is set to 15 V (maximum), see Section 7.6.
	Required voltage exceeds system limits.	Increase pulse width to reduce current requirement.
	Electrode impedance may be too high.	Check impedances and, if high, select a different stimulating electrode if possible (Section 6.4.1). Add more return electrodes.
	CL stimulation is not working as intended.	Check the activation plot, it should be linear and increasing. If it is not, try changing recording or reference electrodes.
Download logs failure.	Download of log file has failed.	Attempt to re-download the logs (Section 6.2.2).
	Ensure 'Factory Reset' has been completed after a firmware upgrade	Perform a 'Factory Reset' (Section 6.7) if you have just completed a firmware upgrade.
Electrode disconnected.	Electrode may be broken, or in highly resistive tissue.	Reprogram using a different electrode. If immediately post-surgey, situation may resolve after 24-48 hours.
	Electrode may be disconnected from intraoperative cable, lead adapter or stimulator.	Remove the proximal connector end from the intraoperative cable, lead adapter (or CLS if permanent implant procedure), clean the contacts and re-insert.
Data won't synchronize/upload and/or reports will not email	Invalid CI	Contact your Saluda Representative to ensure the CI is on the approved list.
	Connection Error	Ensure you have an internet connection.
	Consent is not set appropriately.	Data will not be uploaded and Reports cannot be emailed if the consent has not been set appropriately for the region (see Section 6.3.1).

13. Package contents

Table 13.1: Package contents.

Package	Package Contents
Evoke Clinical Interface (CI) (Ref No.: 3024)	1 x Tablet Computer 1 x Tablet Keyboard 1 x Power Adapter
Evoke Clinical System Transceiver (CST) (Ref No.: 3004)	1 x Clinical System Transceiver (CST)

14. Technical Specifications

14.1 Device Specifications

Refer to the Evoke SCS System User Manual and Evoke SCS System Surgical Guide for device specifications for additional components of the Evoke SCS System.

14.1.1 Evoke CI Tablet specifications

The CI tablet computer has minimum hardware specifications as follows:

Table 14.1: Evoke CI tablet minimum hardware specifications.

RAM	8 GB
Storage	100 GB
USB port	USB 2.0
Display type	Touchscreen
Display size	12.3 inches
WiFi	802.11 a/b/g/n/ac compatible
Camera resolution	4.5 MP

14.1.2 Evoke CST specifications

Table 14.2: Evoke CST specifications.

Materials	Top and bottom cases	ABS Plastic
	Intermediate Ring	TPE
	Cable Sheath	PVC
Dimensions	CST	85 x 53 x 16 mm (3.35 x 2.10 x 0.65 in)
	Cable	1.02 m (3 ft 3.6 in)
Weight	46 g (1.6 oz)	
Power Source	USB port of Evoke Clinical Interface (CI), +5 VDC, 0.5A	
Communications Link	USB connection between laptop and CST. USB port current limit 500 mA MICS band (402–405 MHz) half-duplex radio frequency communication. CST – Master to CLS/eCLS - Slave	
Radio frequency communication	MICS band	402 - 405 MHz
	8 channels*	Centre frequency (MHz): 402.45, 402.75, 403.05, 403.35, 403.65, 403.95, 404.25, 404.55
	Transmit/Receive Channel Bandwidth	300 kHz
	Modulation type	Frequency Shift Keying (FSK)
	Raw Data rate	200kbs
	Antenna type	Internal PCB mounted antenna

	Antenna Gain	-8.7dB (manufacturer's data)	
	Range	1.0 m (3.3 ft.)	
	Effective Isotropic Radiated Power (EIRP)		
		25 µW (-16.02 dBm) maximum	
	FCC ID	2AYGR-3004	
*Channel selection is based on Clear Channel Assessment (CCA) protocol whereby CST, being a Communication Link Master, selects the channel with the lowest interference level before communication session begins.			
Ingress Protection	IP54 Rating for protection against failure from limited dust ingress, and protection against failure from splashing water.		
IEC 60601-1 / EN 60601-1 Classification	Class II Medical Electrical Equipment Continuous Operation Portable Type BF applied part		
Storage & Transportation Conditions	Temperature:	Min: -20 °C (-4 °F)	Max: 60 °C (140 °F)
	Humidity:	Min: 0% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106 kPa (1.05 atm)
Operating Conditions	Temperature:	Min: 5 °C (41 °F)	Max: 40 °C (104 °F)
	Humidity:	Min: 15% RH	Max: 90% RH
	Pressure:	70 kPa (0.69 atm)	Max: 106 kPa (1.05 atm)

14.2 Wireless Communication

14.2.1 Quality of Service & Wireless Coexistence

The Evoke SCS System employs a wireless communication link operating in the 402-405 MHz MICS frequency band. This band is designated for implantable medical devices and enables communication between the CLS/eCLS and the CST or EPC.

At the beginning of each communication session, the CST or EPC automatically scans 8 channels in the frequency band and selects the least congested channel for communication. All communication is error checked and is retried automatically. The user is notified if the wireless communication link fails to connect.

The communication range between the CST/EPC and the CLS/eCLS is typically 1 meter (3.3 feet). If you experience issues with the wireless communication between the CST/EPC and CLS/eCLS, try the following:

- Decrease the distance between the devices.
- Move the devices away from other devices that may be causing interference (see Section 14.3).
- Restart the CPA, wait a few minutes and try connecting again.
- Do not operate other wireless devices, such as a mobile phone, tablet or laptop, at the same time.

14.2.2 Wireless Security

The Evoke SCS System has a communication range of 1 meter (3.3 feet). To enable the CST/EPC to communicate with an eCLS or CLS, it must first be paired with that stimulator. The CST/EPC may communicate with only one CLS or eCLS at a time. The stimulator will not respond to any communication that does not come from a paired device. Additional mechanisms are in place to safeguard the integrity of the communication. There are no security settings that require input or control by the user.

14.3 Electromagnetic Interference

The following tables indicate the electromagnetic environment in which the Evoke SCS System is intended to operate. This is to ensure compliance with international standards for the electromagnetic interference (EMI) produced by the Evoke SCS System, or the susceptibility of the Evoke SCS System to EMI. For more information on this section please contact a Saluda Representative.

⚠**Caution:** Use of accessories, transducers, and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

14.3.1 Guidance and Manufacturer's Declarations

Table 14.3: Electromagnetic emissions.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.		
Emissions Test	**Compliance**	**Electromagnetic environment – guidance**
Radiated disturbance, 30 MHz - 6000 MHz CISPR 11 (EN 55011)	Group 1, Class B	Evoke SCS System is unlikely to produce electromagnetic interference with nearby electronic equipment.
Conducted Emissions 0.15 MHz -30 MHz CISPR 11 (EN 55011)	Class B	Evoke SCS System is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable for the battery powered devices or device consuming less than 75 W from mains power outlet (Charger with power adapter)	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Not applicable for the battery powered devices. Charger with power adapter complies with requirements of the standard	

Table 14.4: Electromagnetic immunity – electrostatic discharge and mains power.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.			
Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic environment – guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV air	±2 kV, ±4 kV, ±6 kV, ±8 kV contact ±2 kV, ±4 kV, ±8 kV, ±15 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%
Electrical fast transient/burst IEC 61000-4-4	± 2 kV gaseous discharge at 100 kHz repetition frequency	± 2 kV @100 kHz repetition frequency for power supply lines to Charger power adapter	Mains power quality should be that of a typical household, commercial or hospital environment. If the user of the Evoke Charger power adapter requires continued operation during mains power interruptions, it is recommended that the Evoke Charger power adapter be powered from an uninterruptible power supply or a battery.
Surge Immunity IEC 61000-4-5	± 0.5 kV, ± 1 kV	± 0.5 kV, ± 1 kV power supply line to Charger power adapter	
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0 % residual voltage; 1 cycle, and 70% residual voltage; 25/30 cycles Single phase: at 0° Voltage Interruptions: 0% residual voltage; 250/300 cycles	Voltage Dips: 0% residual voltage for 0.5 cycle at 0 °, 45 °, 90 °, 135 °, 180 °, 225 °, 270 °, 315 °; 0% residual voltage for 1 cycle at 0 °; 70% residual voltage for 25 cycles at 0 °; Voltage Interruptions: 0% residual voltage for 250 cycles at 0 °; Interval between Events – min. 10 s; Test cycle – 3 times;	
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m 50/60 Hz	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical household, commercial or hospital environment.

Table 14.5: Electromagnetic immunity – radio frequency.

The Evoke SCS System is intended for use in the electromagnetic environment specified below. The patient, doctor or any other user of the Evoke SCS System should ensure that it is used in such an environment.

⚠**Caution:** Portable and mobile RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer to any part of the Evoke SCS System, including the cable, than the recommended separation distance stated below (0.3 m, 12 inches). Otherwise, degradation of the performance of this equipment could result.

⚠**Caution:** Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic environment – guidance
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz; 6 Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz 80% AM at 1 kHz	The Charger power adaptor functioned correctly during the test. Not applicable for a battery-powered device.	The separation distance between an interfering RF transmitter and any Evoke stimulator should be greater than 0.3 m and the maximum power from the RF transmitter should not exceed 2 W or 28 V/m at a distance of 0.3 m.
Radiated RF IEC 61000-4-3	10 V/m 80 MHz to 2.7 GHz 80% AM at 1 kHz	3 V/m for professional healthcare facility environment or 10 V/m for home healthcare environment	
Proximity fields from RF wireless communications equipment	Up to 28 V/m at 0.3 m at specified frequencies (refer Table 9, IEC 60601-1-2)	Tested at up to 28 V/m, devices continued to function during test.	

14.4 Federal Communications Commission (FCC)

14.4.1 Interference Statement for CLS, eCLS, CST, EPC

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
- Consult the dealer or an experienced radio/TV technician for help.

⚠FCC Caution: Any changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate this equipment.

This transmitter must not be co-located or operating in conjunction with any other antenna or transmitter.

The devices in the Evoke System may not interfere with stations operating in the 400.150 - 406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

For MedRadio transmitters operating in the 401-406 MHz band, the following statement applies:

> This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it

will not receive interference or that any particular transmission from this transmitter will be free from interference.

14.4.2 Charger

This device complies with Part 18 of the FCC Rules.

14.4.3 Radiation Exposure Statement

The products comply with the FCC portable RF exposure limit set forth for an uncontrolled environment and are safe for intended operation as described in this manual.

15. Glossary of terms

Table 15.1: Glossary.

Term	Definition	
Accessory Belt	An elastic belt with a pouch to hold an eCLS or a Charger coil.	
Activation (spinal cord activation)	The population of spinal cord nerve fibers, in which ECAPs are initiated in response to stimulation. Activation may be estimated by ECAP amplitude.	
Activation Plot	A plot of activation as a function of stimulus current for one or more postures.	
Activation Plot Levels	Defined activation levels (listed below), reported in ECAP amplitude and stimulation current, collected when measuring the activation plot.	
	Level	**Description**
	Threshold (T)	The activation level at either: • ECAP threshold: when ECAPs are first detectable. • Patient perception threshold: when the patient first feels a change in sensation (e.g. paresthesia, pain relief).
	Comfort	The activation level at which the patient reports a preferred comfortable sensation:
	(C-)	• When increasing stimulation from threshold.
	(C+)	• When decreasing stimulation from maximum.
	Maximum (M)	The activation level the patient could tolerate for no more than approximately one minute.
Anode	A stimulation electrode denoted by the **+** symbol, also referred to as the return electrode. The pulse shape at an anode is the inverse of what's shown for Pulse Shape.	
Artifact	A signal resulting from a stimulus that is not related to neural activity, but interferes with measurement of an ECAP.	
Artifact Estimate	An estimate of the artifact that is extracted from the ECAP signal.	

Term	Definition
Biphasic Pulse	A stimulation pulse consisting of two phases: a positive phase and a negative phase. The pulses are constant current, charge-balanced, rectangular, symmetrical, and the phases are separated by a short programmable interphase gap.
Cathode	A stimulation electrode denoted by the ⎼ symbol, also referred to as the stimulating electrode. This is the electrode type that the Pulse Shape refers to. The percentage of current through this electrode can be configured when there is more than one of them.
Charger	The device that charges the battery in the CLS.
Charger Coil	A circular paddle connected to the Charger that is held over the CLS to charge the CLS battery.
Charger Power Adapter	The power supply adapter for the CLS Charger.
Chronaxie	The minimum pulse width needed for neural activation at twice the rheobase current. Chronaxie is also known as the excitability constant or membrane time constant.
ClearCAP	A feature that can be enabled to modify the circuitry behind the reference electrode to help with artifact mitigation.
Clinical Interface (CI)	A computer loaded with the CPA software, which is used to program the CLS/eCLS.
Clinical System Transceiver (CST)	The device that connects to the CI via USB, and exchanges information between the CI and the CLS/eCLS.
RECAP Viewer	A software application on the CI that can be used to analyze data generated by the Evoke System during a programming session or data downloaded from a stimulator.
Clinical Programming Application (CPA)	A computer program user interface that provides the functionalities required to program and analyze the performance of the CLS/eCLS.
Closed-Loop (CL) Stimulation (see PCLC below)	Stimulation that is automatically adjusted in response to a measured ECAP amplitude to maintain a target activation level. This is also known as ECAP-controlled closed-loop stimulation or (in the Evoke Clarity Programming Application) 'feedback enabled' stimulation.

Term	Definition
Closed-Loop Stimulator (CLS)	An implantable pulse generator capable of ECAP-controlled closed-loop stimulation.
Conduction Velocity (CV)	The speed at which an ECAP propagates along the neural pathway, measured in meters per second (m/s).
Constant Current Stimulation	Stimulation using a current source in which output current is controlled at a fixed level across each pulse.
Dorsal Column	The dorsal region of the spinal cord, which is the primary target of SCS. The dorsal column is made up of Aβ fibers. When they're activated by stimulation, action potentials propagate up and down the Aβ fibers in the dorsal column.
Dorsal Root	The branch of a spinal nerve containing sensory or afferent nerve fibers that travel to the dorsal root ganglion and then enter the spinal cord, travelling to spinal cord tracts such as the dorsal column, or to synapse in the dorsal horn.
Electrode	An electrical contact that may be employed to deliver stimulation current or measure neural responses.
ECAP Amplifier	The measurement amplifier in the CLS/eCLS used to measure ECAPs.
Evoke Patient Controller (EPC)	A remote control that allows the patient to adjust the stimulation output from the CLS/eCLS.
Evoked Compound Action Potential (ECAP)	The measured sum of electrical signals from multiple nerve fibers elicited by an electrical stimulus.
ECAP estimate	An estimate of the ECAP without artifact that is extracted from the ECAP signal.
External Closed-Loop Simulator (eCLS)	A non-implantable pulse generator capable of ECAP-controlled closed-loop stimulation.
Feedback Variable (FBV)	The measured parameter of spinal cord activation used in a closed-loop SCS system. In the Evoke System, the parameter used for FBV is ECAP amplitude.
Histogram	A graphical representation of the distribution of data from the therapy logs (including current, ECAP amplitude and target, over a period of time).
Interphase Gap (IPG)	The delay between phases of a stimulation pulse.

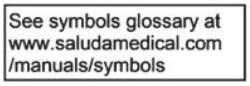
Term	Definition
Intraoperative Cable	Sterilized cable which enables the connection between leads/lead extensions and the eCLS.
Late Response	A neural response resulting from dorsal root activation. Late responses occur after the ECAP and do not propagate along the spinal cord.
Lead	Insulated cable with a number of exposed electrodes at the distal end used in neurostimulation therapy.
Lead Adapter	An adapter that enables the connection between leads/lead extensions and the eCLS.
Lead Extension	Insulated cable that connects to the proximal end of a lead and in turn connects to a lead adapter.
Lead Offset	The vertical alignment of two implanted leads, which may be estimated using the lead offset measurement feature.
Log Files:	Data saved on the stimulator during patient use that can be downloaded by the CPA for analysis with the RECAP Viewer.
Usage Log	A time-stamped record of patient and clinician interactions with the stimulator, and the stimulator status.
Error Log	A time-stamped record of alert and error events associated with stimulation.
Therapy Log	A record of current, ECAP amplitude, and target for each stimulation pulse, accumulated and compressed over fixed time-periods (e.g. every 4 hours), and used to generate histograms.
Maximum Charge Factor	A setting used during the automated chronaxie and rheobase test to determine the maximum stimulation current to be used for each pulse width. The factor is the ratio (0 to 1) between the patient reported maximum current at the initial test pulse width and the equivalent current at infinite pulse width.
Measurement Electrode Scan (MES)	A display feature that can be enabled to allow signals from multiple combinations of measurement electrodes to be displayed simultaneously.

Term	Definition
Measurement Electrodes	Electrodes use in the measurement of an ECAP signal. Comprises the recording electrode and the reference electrode. The measured signal is the difference between what's measured on these two electrodes. "Measurement Electrode" (singular) is sometimes used to refer to just the recording electrode. *See also Recording Electrode and Reference Electrode.*
Neural Response Profile (NRP)	A set of objective measures characterizing a patient's response to spinal cord stimulation.
Open-Loop Stimulation	Stimulation delivered when closed-loop is disabled. The system delivers a fixed-output of stimulation current when closed-loop stimulation is disabled. In the Evoke Clarity Programming Application, this is also known as 'feedback disabled' stimulation.
Paresthesia	Sensation felt by the patient as a result of activation of Aβ fibers by the stimulation pulses.
Physiologic Closed-Loop Controlled (PCLC) Stimulation	Stimulation that is automatically adjusted in response to a measured ECAP amplitude to maintain a target activation level. This is also known as ECAP-controlled closed-loop stimulation or (in the Evoke Clarity Programming Application) 'feedback enabled' stimulation.
Patient Sensitivity	A patient dependent setting that is prescribed by the clinician to optimize closed-loop stimulation.
Program	The complete set of parameters describing stimulation, recording, measurement and feedback. A program may contain up to 4 Stim-Sets.
Recording Electrode	One of the electrodes used in the differential measurement of an ECAP signal, also referred to as R+. This is typically the one placed closest to the stimulation electrodes. *See also Measurement Electrode.*
Reference Electrode	One of the electrodes used in the differential measurement of an ECAP signal, also referred to as R-. This is typically the one placed furthest from the stimulation electrodes. *See also Measurement Electrode.*
Return Electrode	*See Anode.*

Term	Definition
Rheobase	The minimum stimulus current needed for neural activation at an infinitely long pulse width.
Sensitivity	The slope of the activation plot above ECAP threshold measured by the CPA. Sensitivity is a measurement of the sensitivity of the neural response to stimulation current for a given posture and it is used as a guide for the patient sensitivity setting in closed-loop stimulation.
Spinal Cord Stimulation (SCS)	A treatment for chronic pain utilizing pulsed electrical signals delivered to the spinal cord.
Stim-Set	See Stimulation Set
Stimulation	The application of electrical current through electrodes.
Stimulation Electrode	Electrodes use in the delivery of a stimulation pulse. Comprises the cathode(s) and the anode(s).
Stimulating Electrode	*See Cathode.*
Stimulation Set	A set of stimulation parameters designed to target a particular area of the patient's pain. Also referred to as StimSet (in this manual and in the CPA).
Strength Duration Curve	A plot of the threshold current versus pulse width. The strength duration curve represents the excitability of the axons stimulated, or more specifically the excitability of the nodal membranes. It is described by two parameters, rheobase and chronaxie.
Target	The ECAP amplitude that closed-loop stimulation maintains by automatically adjusting stimulation current. The target is set by the clinician and may adjusted by the patient using the EPC.
Therapeutic Window	The therapeutic range of activation, defined by the ECAP amplitudes between threshold and maximum. Therapeutic window represents the range within which dorsal column fiber recruitment is occurring without uncomfortable side effects.
Triphasic Pulse	A stimulation pulse consisting of three phases of alternating polarity. The pulses are constant current, charge-balanced, rectangular, and the phases are separated by a short programmable interphase gap.

16. Symbols

Table 16.1: Symbols.

Symbol	Definition
	Follow the instructions for use at this website: www.saludamedical.com/manuals
	Follow the instructions for use
	Follow the instructions for use at this website: www.saludamedical.com/manuals
	Symbols Glossary can be found on this website: www.saludamedical.com/manuals/symbols
	Caution
	Catalogue number
	Serial number
	Lot number
	Unique Device Identifier
 YYYY-MM-DD	Use by date (YYYY = year, MM = month, DD = day)
	Temperature limitation (°F and °C)
	Manufacturer
 YYYY-MM-DD	Date of manufacture (YYYY = year, MM = month, DD = day)
	Do not dispose of this product in the unsorted municipal waste stream – return to Saluda Medical for disposal
	Type BF applied part
	Non-ionizing electromagnetic radiation

Symbol	Definition
	Do not use if package is damaged
	MR Conditional: Refer to Evoke SCS System MRI Guidelines at https://www.saludamedical.com/manuals
	Magnetic Resonance (MR) unsafe: External components of the Evoke SCS System are MR Unsafe.
	Contents
	Class II Medical Electrical Equipment
	Do not re-sterilize
	Do not re-use
IP22	Ingress Protection Rating 22: • Protected against access of solid foreign objects greater than or equal to 12.5 mm diameter. • Protected against vertically dripping water when the device is tilted 15 °.
IP30	Ingress Protection Rating 30: • Protected against ingress of solid foreign objects greater than or equal to 2.5 mm diameter.
IP54	Ingress Protection Rating 54: • Protected against failure from limited dust ingress. • Protected against failure from splashing water.
FCC ID	An FCC ID is a unique identifier assigned to a device registered with the United States Federal Communications Commission.
Rx Only	Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner

17. Contact us

Most questions you have about programming the Evoke Closed-Loop Stimulator and Evoke External Closed-Loop Stimulator can be answered by reading this manual or looking at our website, www.saludamedical.com and/or www.saludamedical.com/manuals.

If you have any further questions, please contact your Saluda Medical representative. Alternatively, you can contact us via the details below, or email us at info@saludamedical.com.

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