SETPOINT SYSTEM

PRESCRIBER

INSTRUCTIONS FOR USE

Read all instructions, warnings and cautions carefully.

Failure to do so may damage the SetPoint System,
cause it to malfunction or perform poorly, and could result in injury.

If you have any questions about the information contained in the **SetPoint System Prescriber Instructions for Use** (Prescriber IFU), please **contact SetPoint Medical**.

All SetPoint System Instructions for Use (IFUs) are available on the SetPoint Medical website.

If you experience any incident or problem related to the SetPoint System that may pose a safety risk, report it to SetPoint Medical immediately.

Contact

SetPoint Medical Corporation
25101 Rye Canyon Loop
Valencia, CA 91355-5004
United States

setpointmedical.com
+1 661.339.7900
customersuccess@setpointmedical.com

Caution: Federal law restricts this device to sale by or on the order of a physician.

PRESCRIBER QUICK REFERENCE GUIDE

SETPOINT SYSTEM SET-UP

CONFIRM CHARGER FIT

- Prior to the implant procedure, either place the Charger, or instruct the patient to place the Charger around their neck while they are seated upright.
- Verify that the magnetic latch closes and remains latched without discomfort.
- Remove the Charger or instruct the patient to remove the Charger.

See section **Charger Fit Confirmation** for more details.

UNPACK AND ISSUE THE CHARGER

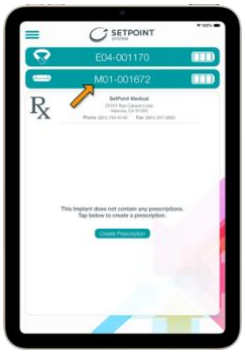
- Unpack the Charger and Docking Station and plug the Docking Station into power.
- Place the Charger briefly on the Docking Station to wake up the Charger. No charging is required.
- Train the patient on how to use their SetPoint System and provide them with the Patient IFU QR code.

See sections **Unpacking and Issuing the Charger** and **Patient Quick Reference Guide** for more details.

CONNECTING PROGRAMMER, CHARGER, AND IMPLANT

1. Place and close the Charger around the patient's neck.
2. Confirm the connection with the Implant; indicated by two beeps that go up in tone and green or orange LED on the Charger.
3. Launch and sign in to Programmer.
4. Press "Select" under the patient's Charger in Programmer.
5. Tap twice on the Charger's magnetic latch to authorize connection; confirmation is indicated by one single long beep.
6. Confirm the Implant serial number matches the patient's record.

See section **Connecting Programmer to Charger and Implant** for more details.



PRESCRIBER QUICK REFERENCE GUIDE

PRESCRIPTION MANAGEMENT

CREATING A PRESCRIPTION

- Connect Programmer, Charger, and Implant.
- Press **Create Prescription** in the Prescription Panel.

See section **Creating the Prescription** for more details.

EDITING A PRESCRIPTION

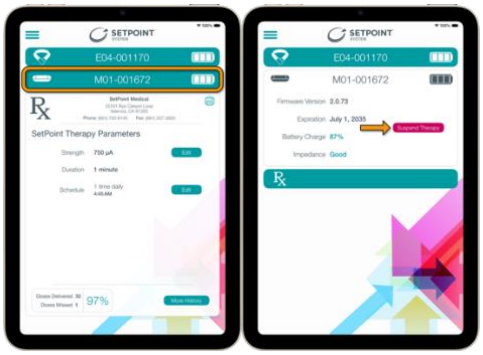
- Press **Edit** to the right of **Strength**.
- Adjust the prescription in 50-250 µA increments to determine a comfortable stimulation strength.
- Test the dose for 15 seconds by pressing **Test Dose Strength**.
- If the test dose is uncomfortable, let discomfort resolve, then decrease the dose strength by 50 µA and retest. Repeat until stimulation is comfortable.
- Accept or reject the dose by pressing **Accept** or **Reject**.
- Save prescription by pressing **Accept** and **Save**.

See section **Adjusting Dose Strength** for more details.

SUSPENDING THERAPY

- Press the Implant Panel.
- Press **Suspend Therapy** and then **Suspend**.
- Ensure the Charger LED shows solid pink.

See section **Suspending Therapy** for more details.



RESUMING THERAPY

- Press the Implant Panel or Prescription Panel and then press **Resume Therapy**.
- When prompted, press **Resume** to confirm.
- Ensure the Charger LED shows green or orange.

See section **Resuming Therapy** for more details.

It is important to read and understand the entire contents of the Prescriber IFU prior to use of the SetPoint System. It is also important to provide the patient with the Patient IFU and to train them on how to use their SetPoint System using section **Patient Quick Reference Guide**. Once training is complete, ask the patient to demonstrate their understanding and provide further training on areas that need reinforcement. Make sure to brief the patient on contraindications and warnings using section **Important Safety Information**.

SETPOINT® SYSTEM

MKT-104.B

PATIENT QUICK REFERENCE GUIDE

SETPOINT SYSTEM USE & CARE

CHARGING CHARGER

- Always place your Charger on the Docking Station when you're not wearing it to keep it fully charged.
- The Charger is fully charged when its LED turns solid green, or when the Docking Station's LED is solid blue.
- Be sure your Charger is fully charged before bringing it to the clinic.

TRAVELING

- Always use the Carrying Case to transport your Charger.
- Do not use your Charger while traveling in any vehicle, including cars, trains, boats, or planes.
- If airport security has questions about your SetPoint System, show them your Patient ID Card.

CLEANING CHARGER

- Clean your Charger with a dry, lint-free cloth, avoiding the magnetic latch.
- To remove lotion or oils, you can use isopropyl alcohol (IPA) wipes–these are also safe for cleaning the magnetic latch area.
- Never spray liquids directly on the Charger or submerge it in any liquid.
- Keep the magnetic latch area free of lint and dirt.

CHARGING IMPLANT

- Wear your Charger around your neck and ensure the magnetic latch is securely closed.
- Charging starts when the LED blinks green or orange, and you hear three beeps that rise in tone.
- Charging is complete when the LED turns solid green and you hear four beeps–three rising tones followed by a repeat of the last tone.
- To stay on track, it's recommended to charge your Implant at the same day and time each week.

Avoid areas marked with radio-frequency (RF) safety warning signs.

Contact your clinic immediately if you experience any pain or discomfort.

Remember to charge your Implant every week

This information is not a substitute for fully reading and understanding the Patient IFU (Instructions for Use). Please refer to the Patient IFU for complete details on how to use the SetPoint System safely and effectively. In addition to reading this guide, please watch the training video here or scan the QR Code.

SETPOINT® SYSTEM

Table of Contents

Introduction

This **SetPoint System Prescriber Instructions for Use** (Prescriber IFU) describes the operation and intended use of the SetPoint System and the process for programming the SetPoint System. The SetPoint System is to be used only by healthcare professionals who have reviewed and understand this Prescriber IFU.

The table below shows the SetPoint System model numbers for the parts of the system that are described in this IFU.

Device Name	Model Number
Implant	M01
Charger	E04
Docking Station	C01

Table 1 - Device Names and Model Numbers

Indication for Use

The SetPoint System is indicated for use in the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response, loss of response or intolerance to one or more biological or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs).

Pediatric Use

The SetPoint System is not intended for use in the pediatric population.

SetPoint System Description

The SetPoint System includes:

- The Implant (A) which is placed within a Pod (B) and implanted on the left vagus nerve in the neck (C)
- A Charger (D) with Docking Station (F)
- A Programmer (E)

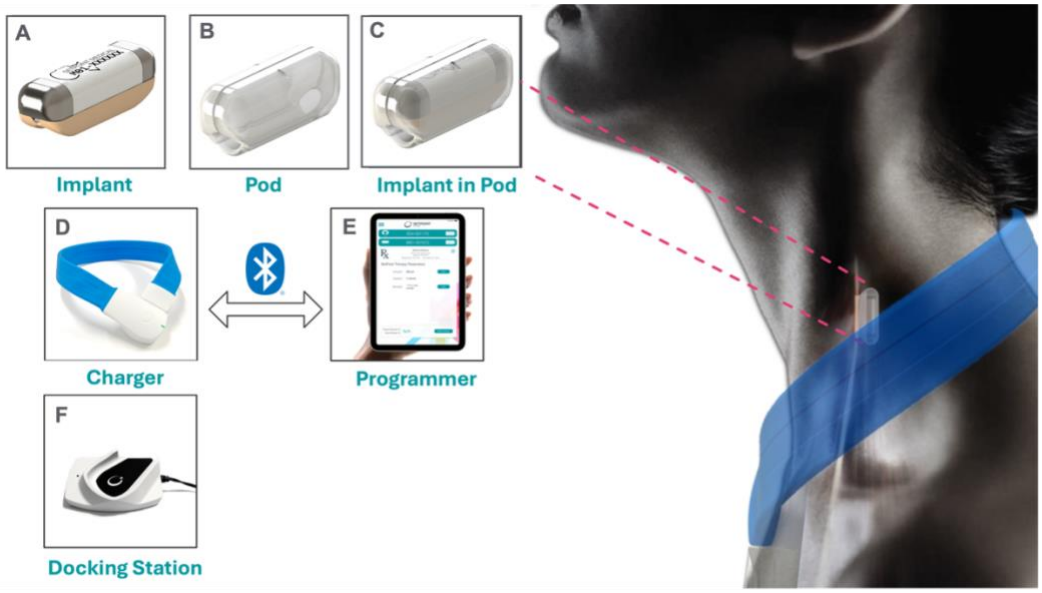


Figure 1 - SetPoint System and Components

Implant and Pod

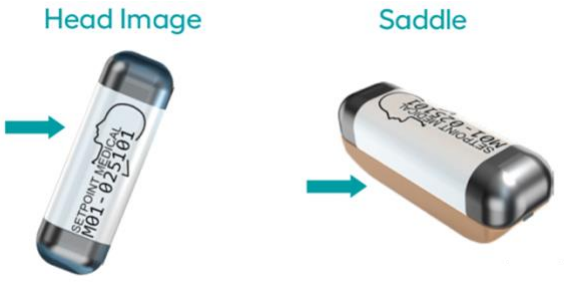


Figure 2 - Implant

The Implant is an integrated neurostimulation device. It is used to electrically stimulate the vagus nerve for 1 minute, every day. It is about 1 in (2.5 cm) long and weighs about 0.1 oz (3 g). An experienced surgeon implants it next to the vagus nerve on the left side of the neck. The Implant is placed inside a Pod, which is a flexible cover made of silicone. The Pod helps hold the Implant in place.

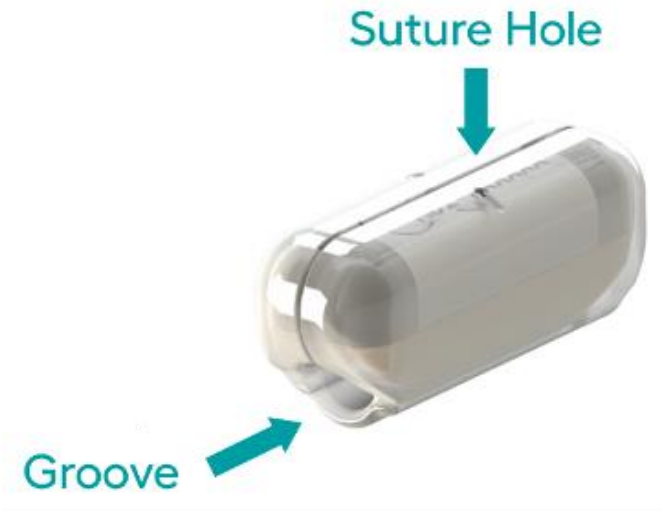


Figure 3 - Pod

For more information regarding the use of the Implant or Pod, please refer to the **SetPoint System Surgeon Instructions for Use** available on the SetPoint Medical website.

Charger

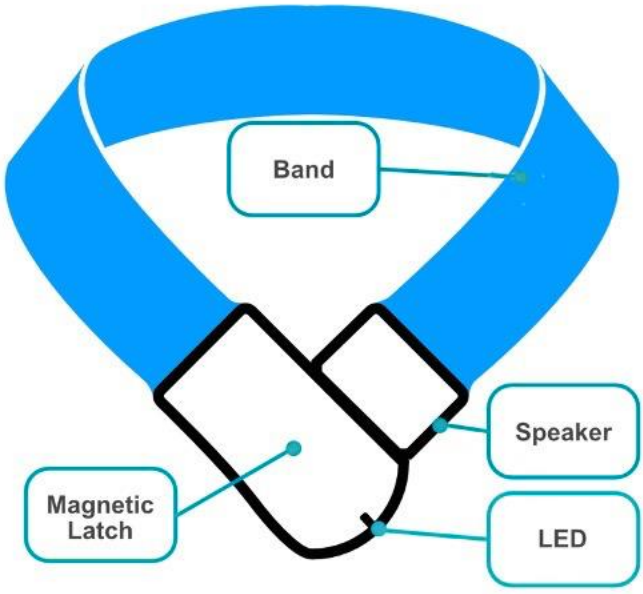


Figure 4 – The Charger

The Charger is a device worn around the patient's neck. It is used for charging the Implant at home and for programming the Implant at the clinic. It is recommended to be worn once a week to charge the Implant.

The Charger is about 24 in (61 cm) long and 1.5 in (3.8 cm) wide, when unlatched and laid flat, and weighs about 9 oz (270 g). The Charger does not have any buttons or switches, but it does have an LED and a speaker.

The Charger only comes in one size that is meant to fit most people, forming a circular ring about 21 in (53 cm) in circumference when latched. Before the implant procedure, it is necessary to perform a fit and tolerability test on the patient. This makes sure it fits comfortably around their neck and that the magnetic latch closes.

Docking Station

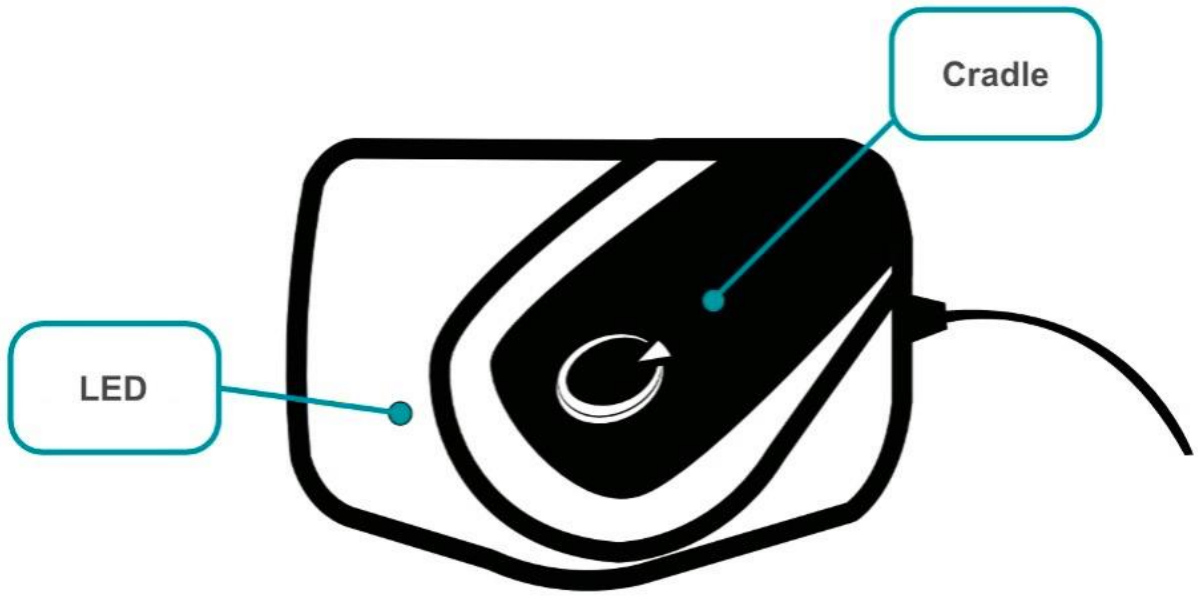


Figure 5 – The Docking Station

The Docking Station is provided with the Charger. The Docking Station is for charging and storing the Charger. Only the Docking Station provided in the Carrying Case should be used to charge the Charger. Use of any other wireless power supply may damage the Charger, the wireless power supply, or both.

The Docking Station is about 4.5 in (11.4 cm) wide, 3 in (7.6 cm) deep, and 2 in (5.0 cm) tall, and weighs about 10 oz (290 g). The Docking Station does not have any buttons or switches, but it does have an LED. The Docking Station has a cradle for placing the Charger on and a power cord that must be plugged into an electrical outlet. The Docking Station cannot be serviced at home or in the clinic. The Docking Station is meant to be used indoors and should always stay plugged in.

Carrying Case

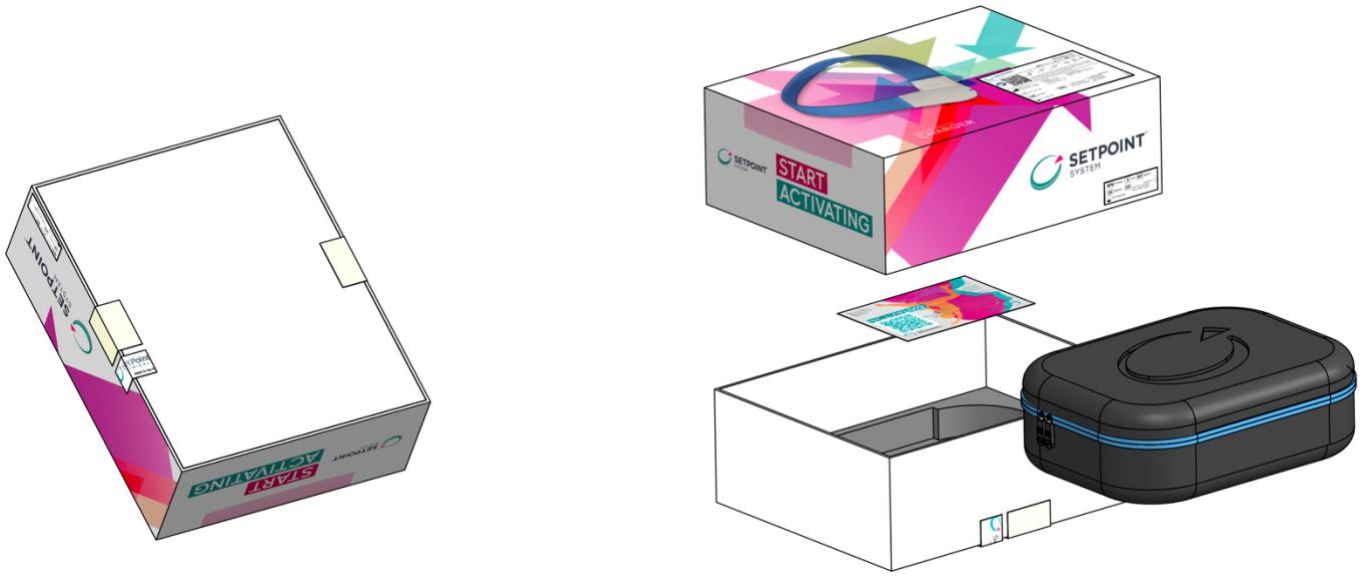


Figure 6 – Carrying Case Inside Sealed Product Box

The Charger and Docking Station are provided in a Carrying Case shipped inside of a product box. The product box is sealed with tamper evident labels. See **Unpacking and Issuing the Charger** for instructions on how to unpack the Charger.

Programmer

Programmer is an app installed on an Apple iPad® that is only used by a trained healthcare professional. It is used with the Charger to program the Implant or to turn off or resume stimulation, if necessary. Additionally, it gives the healthcare professional information about the use of the Implant and Charger, such as how many doses have been delivered or missed, and Implant battery charge levels.

Patient Identification (ID) Card

The Patient ID Card, shown in **Figure 7**, is included in the Implant packaging. The Patient ID Card is filled out and provided to the patient after the surgery, and before they leave the hospital. Patients should be instructed to always have their Patient ID Card on hand and present it during security screenings, such as at airports. Additionally, the QR code on the card provides access to critical information regarding the Implant, which is necessary to ensure that any treatments are compatible with it. Instruct the patient to always present the Patient ID Card to healthcare professionals and providers such as physicians, dentists, imaging technicians (e.g., MRI, X-ray, computerized tomography), physical or occupational therapists, estheticians and beauty-care specialists before pursuing any additional medical, medical imaging or beauty treatments. Neglecting to inform these professionals about the Implant may cause harm to the SetPoint System and/or may lead to complications with the treatment. If the patient changes their doctor or rheumatologist managing the SetPoint System, or loses their card, they should **contact SetPoint Medical for a replacement card**.

Figure 7 - Sample Patient ID Card (Front and Back)

Important Safety Information

Read all instructions, warnings and cautions carefully. If you have any questions, **contact SetPoint Medical**. If the patient does not follow these guidelines, the SetPoint System could get damaged, not work correctly, and/or result in harm.

Contraindications

There are certain situations in which the SetPoint System should not be used because the risk(s) are greater than the potential benefit(s).

The SetPoint System should not be used:

- If the patient has had certain health procedures that would interfere with how the device works, for example,
  - If they have had surgery to remove the vagus nerve (vagotomy).
  - If they have had their spleen removed (splenectomy).
- If you determine that it might not be safe for them to have the surgery, for example,
  - If they have spine disease in their neck that makes it risky to place a breathing tube (intubate).
  - If they cannot be safely given anesthesia for surgery.
- If they cannot safely use the SetPoint Charger, for example,
  - If their neck is too large to wear the SetPoint Charger.
  - If they have a pacemaker or a defibrillator implanted.

Warnings & Precautions

It is important that the patient use the SetPoint System safely to avoid injury or damage to the SetPoint System or other devices. Here are some key safety tips:

- Instruct the patient to always present the Patient ID Card, prior to undergoing any treatment or diagnostic procedure, to healthcare professionals and providers such as physicians, dentists, imaging technicians (e.g, MRI, X-ray, computerized tomography), physical or occupational therapists, estheticians and beauty-care specialists. Failure to present the Patient ID Card may result in a treatment or procedure-related complication and/or may damage the SetPoint System (see **Medical Imaging Warnings** below).
- Instruct the patient not to scuba dive or enter a hyperbaric chamber after receiving the Implant. The safety of high pressure has not been established, and these conditions could damage the device.
- Instruct the patient not to use the SetPoint Charger while it is covered (e.g., with a scarf or similar material), in direct sunlight, or in air temperatures exceeding 90 °F (32 °C). If they do, it may cause the Charger to rapidly overheat and prematurely shut down.
- Instruct the patient not to continue to use the SetPoint System beyond its expected service life. The Charger and Docking Station each have a 5-year service life. Use after 5 years can lead to additional risks associated with device deterioration over time. Signs of performance degradation include incomplete Implant charging during the weekly session. The Implant has a 10- year service life, after which time it will stop providing daily stimulation, it will no longer recharge, and the Implant will need to be replaced.
- Do not use the SetPoint Charger or Docking Station if any cracks, defects, or breaches are present, or if the product box or Carrying Case are badly damaged. If you do, damaged internal electrical components could alter the Charging or Docking Station function or bypass safety features and result in harm.

- Instruct the patient not to use third-party wireless chargers with the SetPoint Charger or try to charge other devices with the SetPoint Docking Station. Using incompatible accessories with the SetPoint System could lead to device damage or malfunction.
- Instruct the patient not to position the SetPoint Charger around the neck if there are any unhealed wounds. If they do, it increases the risk of infection.
- Instruct the patient not to apply excessive force to the SetPoint Charger or handle it roughly. If they do, it may damage its internal electrical components, potentially causing malfunction.
- Instruct the patient not to use any cleaning product on the SetPoint Charger other than isopropyl alcohol (IPA). If they do, it could damage the Charger or leave harmful or irritating residues.
- Instruct the patient to adhere to local e-waste regulations when disposing of any part of the SetPoint System. If they do not, environmental contamination with hazardous substances can result.
- Instruct the patient not to modify or tamper with the SetPoint Charger or Docking Station. If they do, it could alter their function or bypass safety features and result in harm.

Medical Imaging Warnings

There are various types of medical imaging technologies in common use. Although X-rays, computed tomography (CT), ultrasound imaging (sonography), positron emission tomography (PET) are all safe to perform after the patient receives their Implant, it is vital that they always show their Patient ID Card to any healthcare professionals performing these procedures. Specifically for magnetic resonance imaging (MRI), the patient must wait a minimum of two weeks after implantation before they are permitted to have an MRI scan. However, all MRI scans performed more than 14 days after implantation must meet the conditions outlined in the **SetPoint System Magnetic Resonance Imaging (MRI) Safety Information Manual**. This includes the fact that MRI scans must not overlap the time of stimulation of the Implant, which can be avoided by not performing the scan within ±1 hour from the time documented on the patient's Therapy Parameters Card. Note that if the Implant is suspended or expired, it will not deliver stimulation and this restriction is unnecessary. **In any case, as long as the patient is implanted, they must inform MRI personnel that the Implant is *MR Conditional*.**

Figure 8 - MR Conditional

⚠ **Warning: The SetPoint Charger and SetPoint Docking Station should never be brought near MRI machines because they are not safe for use in that environment. Thus, the Charger and Docking Station are referred to as MR Unsafe.**

Figure 9 - MR Unsafe

Medical Procedure Warnings

Instruct the patient to use caution with any medical procedure that introduces electrical current, electromagnetic radiation, or thermal energy into tissues in the neck area. The Implant may absorb, intensify, or reflect these energy sources, resulting in localized heating that could damage the device or nearby nerves and vascular structures. This damage may result in pain or discomfort, loss of vocal cord function, or possibly even life-threatening injury if there is damage to a blood vessel. Note that these risks are present whether the Implant is active or suspended. It is extremely important that they always show

their Patient ID Card to any healthcare professional performing these procedures so that they can carefully evaluate potential risks due to interactions between the procedure and the SetPoint System. Before proceeding with any procedure that delivers energy to the tissues surrounding the Implant, the healthcare professional should consider alternatives that avoid energy transfer. Specific examples of higher risk procedures around the implantation site that need to be avoided because they could damage the Implant, cause it to malfunction, and/or result in harm including severe injury include:

⚠ **Warning:** Shortwave diathermy, microwave diathermy, ultrasound diathermy or other procedures that induce heat in internal tissues. This does not include diagnostic ultrasound which is permitted.

⚠ **Warning:** Electrosurgery/electrocautery, and ablative surgical techniques that utilize any form of electromagnetic radiation or electrical current to cut, coagulate, or thermally destroy tissues. For electrocautery, do not use within 2 cm of the Implant[1]. If using monopolar electrocautery, place the return pad such that the current path is not across the Implant.

⚠ **Warning:** Transcutaneous electrical nerve stimulation (TENS), electroconvulsive therapy or other procedures that apply electrical current through skin surface electrodes.

⚠ **Warning:** Extracorporeal shock wave lithotripsy or other procedures that use pressure waves or induce mechanical forces to break up internal structures.

⚠ **Warning:** Radiation therapy, including forms of photon beam radiation therapy such as x-rays, gamma rays, proton beam therapy, brachytherapy, stereotactic radiosurgery, cobalt machines, and linear accelerators.

If the patient has had any of the above medical procedures around the implantation site, it is very important that, very soon thereafter, they discuss the procedure with their doctor or rheumatologist managing the SetPoint System in order for them to determine whether verification of Implant functionality is necessary.

Radio Frequency (RF) Warnings

The SetPoint System uses radio-frequency (RF) fields for communication between different parts of the system or when charging the Implant or Charger. These RF fields could disrupt the functioning of similar frequency-utilizing devices.

⚠ **Warning:** Instruct the patient not to use the Charger for charging the Implant near devices sensitive to RF interference, while travelling in vehicles such as cars, trains, boats, airplanes, or during any medical treatments, or in proximity to other medical devices.

⚠ **Warning:** The SetPoint System has not been tested with, and may affect the operation of, other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include, but are not limited to, sensing problems and inappropriate device responses.

---

[1] Safety testing was performed using 3 applications of 25 W bipolar and 30 W monopolar electrocautery each at 1 cm from the Implant. Exceeding this number of applications or power setting near the Implant may increase the risk of nerve injury or device failure.

⚠ **Warning:** The RF signals from the Charger could theoretically interfere with or be concentrated by other implanted devices such as neural stimulators or insulin pumps.

The Charger and Docking Station are vulnerable to electromagnetic interference from devices that emit RF fields, like cellphones and security scanners. Portable RF communications equipment (including peripherals such as antenna cables and external antennas), RFID scanners and card readers (including animal identification tag scanners) should be used no closer than 12 inches (30 cm) to any part of the Charger and Docking Station. Otherwise, degradation of the performance of this equipment could result.

⚠ **Warning:** If it is suspected that the Charger or Docking Station are not functioning correctly due to electromagnetic interference, try changing the patient's location, waiting until a later time, or turning off the suspected source of interference if possible. Use of the Charger or Docking Station adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, the Charger and Docking Station should be observed to verify they are operating normally.

⚠ **Warning:** The Charger and Docking Station are intended for use indoors, for example in the home or clinic. They should not be used in environments where the intensity of electromagnetic disturbances is known to be high, such as near high-frequency surgical equipment or radio transmitters. They should also not be used in any environment with a posted FCC Notice, Caution or Warning sign indicating the presence of high-intensity radio frequency (RF) fields that surpass normal public exposure limits. These areas are typically indicated by restricted environment signs like those in **Figure 10**. After receiving the Implant, the patient should not enter these areas without seeking medical guidance first. Exposure to high levels of RF could cause the Implant to malfunction or lead to tissue damage in the vicinity of the device.

Figure 10 - Restricted Environment Signage

Other Help Using the SetPoint System

In addition to the information provided in this Prescriber IFU, supplementary training materials including, but not limited to, a training presentation and programming videos are available and can be provided upon request. Additional training, if requested, can be arranged with your local SetPoint Medical representative.

Using the SetPoint System

The table below shows the conditions for transport, storage, and use of the Charger and Docking Station.

Use	Temperature	Humidity	Altitude
Transport: In Carrying Case	50 to 104 °F (10 to 40 °C)	15 to 93 %RH	Up to 98,425 ft (30,000 m)
Storage: Charger on Docking Station			Up to 9,843 ft (3,000 m)
Use: Charging the Implant	50 to 90 °F (10 to 32 °C)		

Table 2 – Transport, Storage, and Use Conditions

⚠ **Warning:** Instruct the patient not to scuba dive or enter a hyperbaric chamber after receiving the Implant. The safety of high pressure has not been established and these conditions could damage the device.

⚠ **Warning:** Instruct the patient not to use the SetPoint Charger while it is covered (e.g., with a scarf or similar material), in direct sunlight, or in air temperatures exceeding 90 °F (32 °C). If they do, it may cause the Charger to overheat rapidly and shut down prematurely.

The Charger normally heats up during use, potentially reaching up to 118 °F (48 °C). To prevent overheating and premature shutdown, the Charger needs to be at or below 90 °F (32 °C) before being used to charge the Implant. If the Charger has been stored above 90 °F (32 °C), it must be allowed to cool down to this temperature, which can take up to 10 minutes.

⚠ **Warning:** Instruct the patient not to continue to use the SetPoint System beyond its expected service life. The Charger and Docking Station have a 5-year service life. Use after this time can lead to additional risks associated with device deterioration over time. Signs of performance degradation include incomplete Implant charging during the weekly session. The Implant has a 10- year service life, after which time it will stop providing daily stimulation and will no longer recharge. At that time, the Implant will need to be replaced.

The rechargeable battery in the Charger is rated to last for at least 5 years. If the patient cannot complete the weekly Implant charging session with a fully charged Charger, the entire Charger may need to be replaced as its battery cannot be replaced or serviced at home. **Contact SetPoint Medical** if you believe there are any issues with the Charger.

The rechargeable battery in the Implant is rated to last for 10 years. After this point, the Implant is considered expired. It will need to be replaced because it will no longer deliver daily stimulation, and the battery will no longer charge. The entire Implant will be replaced because the Implant's battery cannot be changed. You will be able to determine this by looking at information provided by Programmer during a clinic visit (see section **Implant Expiration**). **Contact SetPoint Medical** if you believe there are any issues with the Implant.

Charger Fit Confirmation

To confirm fit of the Charger prior to the implantation procedure, the following steps shall be performed:

1. Prior to the implant procedure, either place the Charger, or instruct the patient to place the Charger around their neck while they are seated upright.
2. Verify that the magnetic latch closes and remains latched without discomfort.

3. Remove the Charger or instruct the patient to remove the Charger.

Automatic Prescription Dosing

The Implant is programmed with an automatic prescription, relying on the Implant's built-in timer to maintain the dosing schedule. When the Implant is delivering stimulation to the vagus nerve, the patient may or may not feel a sensation near the location of the Implant. Instruct the patient to **contact the clinic** if the stimulation becomes uncomfortable, and the clinic personnel should adjust the prescription based on their comfort level.

Unpacking and Issuing the Charger

The Charger and the Docking Station will be issued to the patient in a Carrying Case (see **Figure 11-3**). The Charger is shipped in a deactivated state to preserve the battery life and must be placed on the Docking Station to take it out of shipping mode prior to the first use. This Carrying Case should be used whenever the patient is transporting the Charger. At home, the patient should unpack the Charger and Docking Station, plug the Docking Station into an electrical outlet, and place the Charger on the Docking Station.

⚠ **Warning:** Do not use the SetPoint Charger or Docking Station if any cracks, defects, or breaches are present, or if the product box or Carrying Case are badly damaged. If you do, damaged internal electrical components could alter the Charging or Docking Station function or bypass safety features and result in harm.

Figure 11 - Unpacking Charger and Docking Station

1. Cut the tape to open the product box.
2. Remove the Carrying Case and Patient IFU QR code from the product box and provide the QR code to the patient.
3. Place the Carrying Case on a flat surface with the logo on top and the handle facing away from you.
4. Unzip the Carrying Case and flip the top open.
5. Remove the Charger from the Carrying Case and set it aside.
6. Remove the Docking Station from the Carrying Case.
7. Uncoil the power cord and plug the Docking Station into an electrical outlet.
8. Place the Docking Station on flat surface, with enough room to accommodate the Charger once placed on the Docking Station and where you can ensure that the Docking Station is at least 8 in (20 cm) away from you during use.
9. Confirm that the Docking Station has a **solid pink** LED before placing the Charger on the Docking Station. If the LED is not showing a **solid pink** light, see **Appendix D – Troubleshooting**.

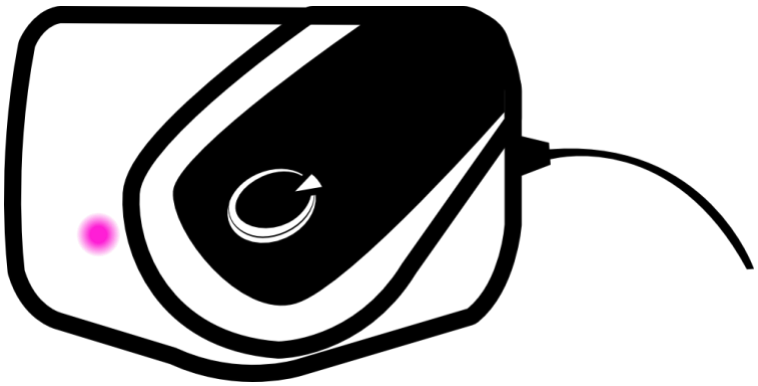


Figure 12 - The Docking Station shows a solid pink LED when it is plugged in, but not charging the Charger.

10. After confirming the Docking Station has a **solid pink** LED it is ready to use. It is best to leave the Docking Station in a location where it does not need to be moved.
11. Place the Charger briefly on the Docking Station to take it out of shipping mode. No charging is required.

Charging the Charger

⚠ **Warning:** Instruct the patient not to use third-party wireless chargers with the SetPoint Charger or try to charge other devices with the SetPoint Docking Station. Using incompatible accessories with the SetPoint System could lead to device damage or malfunction.

The Charger should be placed on the Docking Station whenever it is not being transported or used to charge the Implant (whenever it is not being worn).

1. Place the Charger on the Docking Station's cradle as shown, ensuring the Charger is latched closed. The Charger must be latched while charging.

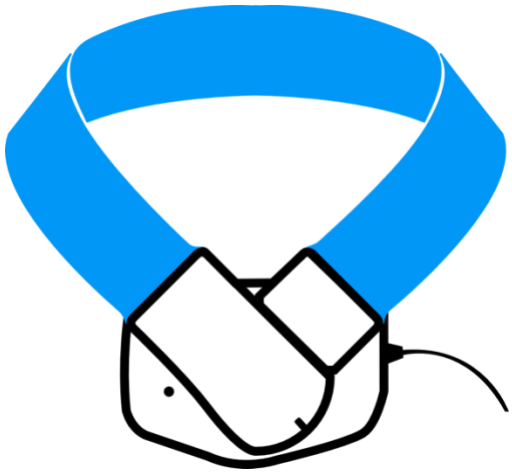


Figure 13 - The Charger must be latched closed when placed on the Docking Station's cradle.

2. The Docking Station's LED will begin **blinking blue** to show that it is charging. If the Charger is fully charged, the Docking Station's LED will display **solid blue**. If the Docking Station does not show a **blinking** or **solid blue** LED, see **Appendix D – Troubleshooting**.

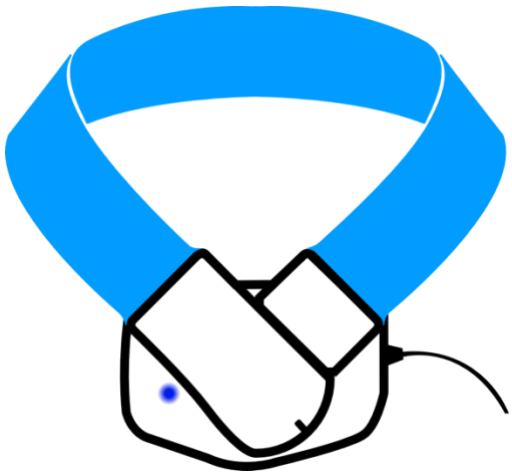


*Figure 14 - The Docking Station's LED **blinks blue** when charging the Charger or shows **solid blue** when charging is complete.*

3. While the Charger is placed on the Docking Station's cradle, tapping on the Charger logo will show its state of charge. If the Charger LED shows **solid green**, it is done charging. If the Charger LED shows **blinking green**, it has enough charge to charge the Implant. If the Charger LED shows **blinking orange**, it is charging but not ready yet to charge the Implant.

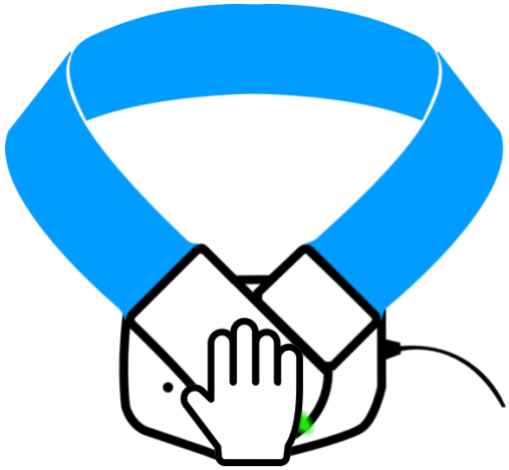


Figure 15 - Tapping on the Charger while it is on the Docking Station will show its state of charge.

Even if the Charger is done charging, there is no need to take it off the Docking Station. Leaving the Charger on the Docking Station ensures that it is always fully charged.

Before the patient visits the clinic or charges their Implant, they should make sure their Charger has a full charge by tapping on the Charger logo while it is on the Docking Station and looking for a **solid green** LED.

Charging the Implant

Once the Implant has been programmed, it is recommended the Implant be charged each week using the Charger. There is no need to charge the Implant prior to initial programming.

⚠ **Warning:** Do not position the SetPoint Charger around the neck if there are any unhealed wounds. If you do, it increases the risk of infection.

The Charger is only to be placed on skin without cuts or wounds. If the Charger needs to be used on an open wound, the wound should be covered in sterile gauze or bandage first.

For ease of use, the Charger has both an LED and a speaker for showing charge status. If needed, patients can use a mirror to look at the Charger LED.

1. Tap on the Charger logo while it is on the Docking Station and look for a **green** LED. If the LED is **orange**, leave the Charger on the Docking Station until it turns **green**.
2. Remove the Charger from the Docking Station.
3. Unlatch the Charger by pulling or twisting the two halves of the magnetic latch apart. Do not touch the pins on the inside of the magnetic latch.
4. Carefully lift the Charger over the patient's head or bring it around their neck. The magnetic latch should rest on the front of the patient's neck with the SetPoint logo half on their right side.
5. Take both halves of the magnetic latch and press them together. The magnets in the Charger should snap into place and latch easily. If the Charger is hard to latch, it is likely twisted or upside down.
6. Make sure the latch is securely closed so the Charger will not fall off. Adjust it so it sits comfortably on the patient's neck.

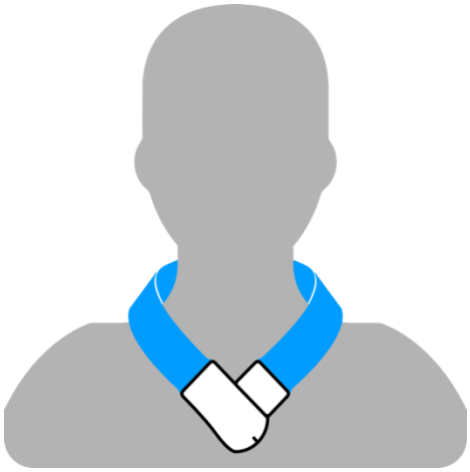


Figure 16 - The Charger should rest comfortably around the neck as shown.

7. The Charger's LED will begin to **slowly pulse white** while it is trying to connect to the Implant. Once it has connected to the Implant, the Charger will play **two beeps that go *up* in tone**. If at any time after connection it plays **two beeps that go *down* in tone**, it means the Charger has lost connection with the Implant.
8. The Charger will play **three beeps that go *up* in tone** when it begins charging the Implant and will then display an **orange** or **green** LED.
9. It is recommended that the Implant be charged for approximately 5 minutes per week or until the battery is full, whichever comes first. The Charger's LED shows **solid green** and plays **four beeps (three beeps that go *up* in tone and a fourth beep that is a repeat of the last tone)** when the Implant battery is full. After the Implant has reached full charge, the beeps will repeat every 30 seconds until you take the Charger off.
10. Once charging is completed, unlatch the Charger and remove it from the patient's neck.
11. Latch the Charger and place it back on the Docking Station.

Following a Routine

Creating a routine can make it easier to remember when to charge the Charger and Implant. SetPoint Medical recommends the following routines:

1. The patient should wear the Charger to charge their Implant for about 5 minutes on the same day each week. For example, they may choose to charge the Implant every Sunday morning or right before going to bed every Saturday night. Less frequent charging may require longer time to fully charge the Implant
2. When not wearing the Charger, it should be placed on the Docking Station. This makes sure that the Charger always has a full charge when it is needed for charging the Implant or for a clinic visit.

Traveling With and Packing the Charger and Docking Station

⚠ **Warning:** Do not apply excessive force or rough handling to the SetPoint Charger. If you do, it may damage its internal electrical components, potentially causing malfunction.

When at home, it is important to follow the recommended routine outlined above to maintain the devices' batteries. When traveling, the patient should consult you on what equipment they should take with them depending on the length of their trip. If they need to bring the Charger or Docking Station, they should always use the Carrying Case.

The patient should bring their Charger to the rheumatologist visit as it may be needed to adjust the programming on their Implant. If they are planning a long trip that requires the Docking Station, they should bring a standard plug adapter if traveling internationally.

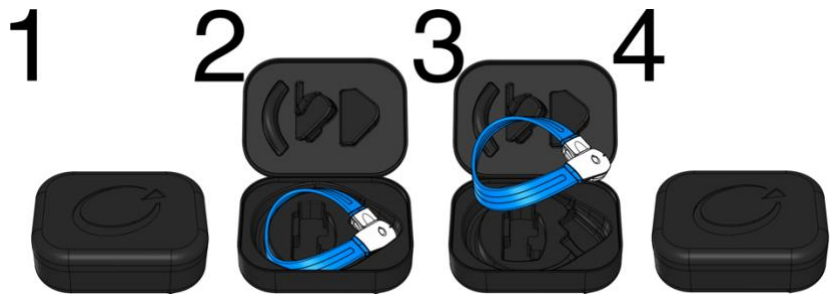


Figure 17 – Packing the Charger in the Carrying Case

1. Place the Carrying Case on a flat surface with the logo on top and the handle facing away.
2. Unzip the Carrying Case and flip the top open.
3. Place the latched Charger in the Carrying Case.
4. Zip the Carrying Case shut.

The Charger cannot be turned off, but it switches to low power mode by itself after about 1 minute of inactivity. Opening or closing the Charger or removing the Charger from the Docking Station will wake it up, and it will begin looking for an Implant.

The patient should pack the Carrying Case in their carry-on luggage when traveling in an airplane. They should provide their Patient ID Card to security personnel when going through airport security if they have any questions or concerns about the SetPoint System. See https://www.tsa.gov for more information about traveling with medical equipment.

Cleaning

⚠ **Warning:** Instruct the patient not to use any cleaning product other than isopropyl alcohol (IPA) wipes to clean the SetPoint Charger. If they do, it could damage the Charger or leave behind harmful or irritating residues.

- Use a dry, lint-free cloth to clean the Charger avoiding the magnetic latch.
- If needed, use isopropyl alcohol (IPA) wipes to clean lotion and oils off the Charger and to clean the magnetic latch area.
- Never spray the Charger with any substance or put it in any liquid.
- Keep lint and dirt out of the Charger's magnetic latch area.

Replacement and Disposal

⚠ **Warning:** Instruct the patient to adhere to local e-waste regulations when disposing of any part of the SetPoint System. If they do not, it can result in environmental contamination with hazardous substances.

To reorder the Charger or Docking Station, **contact SetPoint Medical** and request Catalog Number 90007. The Docking Station is not sold separately from the Charger. Please dispose of the Charger and Docking Station per local e-waste regulations.

Guidelines for Patient Follow-up

Following the implant procedure, the patient should be cleared for programming of the SetPoint System after confirming incision healing, and post-operative recovery. The Implant can be programmed in the Prescriber's clinic. Programming should be performed based on instructions in the **Programming the SetPoint System** section.

At subsequent follow up visits the Prescriber can interrogate the SetPoint System to review prescription history, including percentage of scheduled doses delivered and battery charge (see section **Patient Prescription History**). The SetPoint System interrogation is performed following the steps outlined in **Connecting Programmer to Charger and Implant**.

Subsequent follow-up schedule should be determined by the Prescriber based on patient response to and tolerance for therapy.

Patient Counseling Information

Patients should be counseled to always carry and present the Patient ID Card to healthcare professionals and providers such as physicians, dentists, imaging technicians (e.g., MRI, X-ray, computerized tomography), physical or occupational therapists, estheticians and beauty-care specialists before pursuing any additional medical, medical imaging or beauty treatments. Failure to present the Patient ID Card may result in a treatment or procedure-related complication and/or may damage the SetPoint System (see sections **Patient Identification (ID) Card** and **Medical Imaging Warnings**). If the patient or healthcare professional requires the stimulation to be suspended, the patient should **contact the Prescriber's office**.

Patients should be counseled to establish a routine to charge their Implant on the same day and time every week. When not charging the Implant, patients should be counselled to keep the Charger on the Docking Station to keep it fully charged, and bring a fully charged Charger to the clinic.

In case of uncomfortable side effects, adverse events or device malfunction, the patient must be counseled to immediately notify the Prescriber for further device interrogation and follow-up.

Setting Up to Use Programmer

Programmer is an iPad application that is used to program and interrogate the SetPoint System. An internet connection is required (see section **Troubleshooting Network Connectivity** for details) for installation and use of Programmer. All patient data is stored securely in the Cloud, so Programmer on any iPad can be used for programming and interrogating any Implant using any Charger. For storage and handling of the iPad, refer to the iPad Owner's Manual, or check Apple support at https://support.apple.com.

Understanding Programmer's User Interface

The main components of the interface are the following (see **Figure 18**):

1. **Menu Icon**: used to modify a logged-in user's account, view clinic's prescription history, view application information, and log out of application
2. **Charger Panel**: used to select and initiate connection to a Charger; view Charger information, serial number, firmware versions, and battery state of the Charger
3. **Implant Panel**: used to view Implant information, serial number, firmware version, battery state of the Implant, and impedance status; suspend and resume therapy
4. **Prescription Panel**: used to create, modify, and print prescriptions; view adherence data

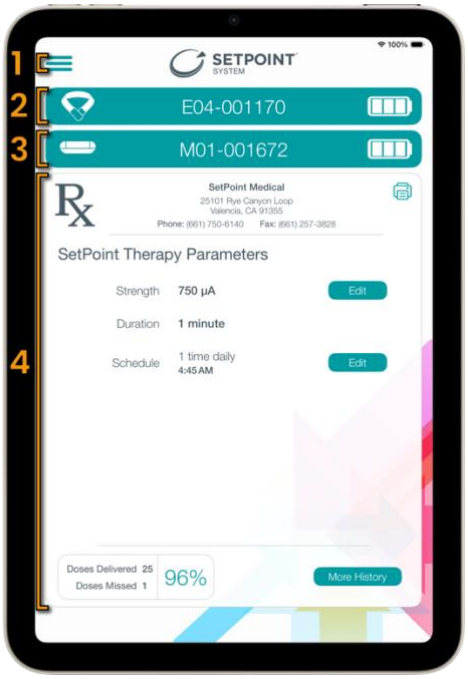


Figure 18 - Locating Programmer's Application Panels

Downloading Programmer

Programmer can be installed on any iPad capable of running the latest version of iPadOS. If the iPad already has Programmer installed, the following download steps should be skipped.

1. Navigate to Apple's App Store from your iPad and search for "SetPoint Programmer".
2. Select "Get" in the App Store.
3. Follow the instructions on the iPad to install the application.

Creating an Account

Before healthcare professionals can connect to the SetPoint System with Programmer, they will need to create a SetPoint Medical account and have that account approved by SetPoint Medical. Each healthcare professional should have their own, unique SetPoint account. A SetPoint account may be created using an email address and password/passkey or by signing in with an existing sign-in provider (e.g., Microsoft or Apple).

1. Press the application icon to launch Programmer.

Figure 19 - Programmer Application Icon

2. To create an account with an email address and password or passkey, press “Create SetPoint Account”.

Figure 20 - Create SetPoint Account

3. Enter the email address and name you wish to have associated with your SetPoint Medical account and press “Create SetPoint Account”.

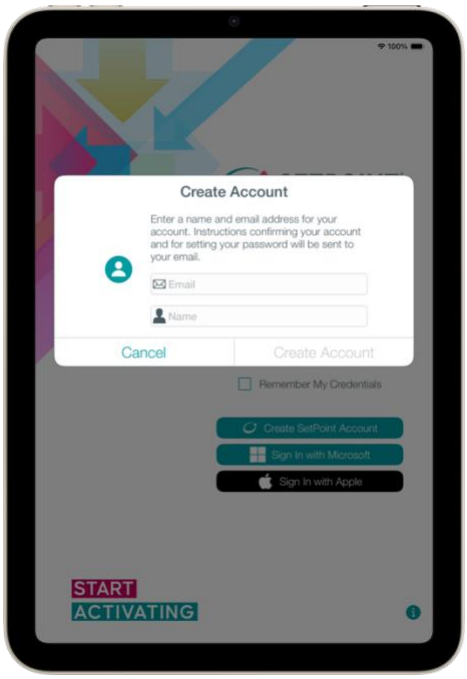


Figure 21 – Enter Email and Name

4. Once your account has been created, you will be prompted to verify your email. An email will be sent to the email address provided during account creation, and it must be verified before you may sign in.

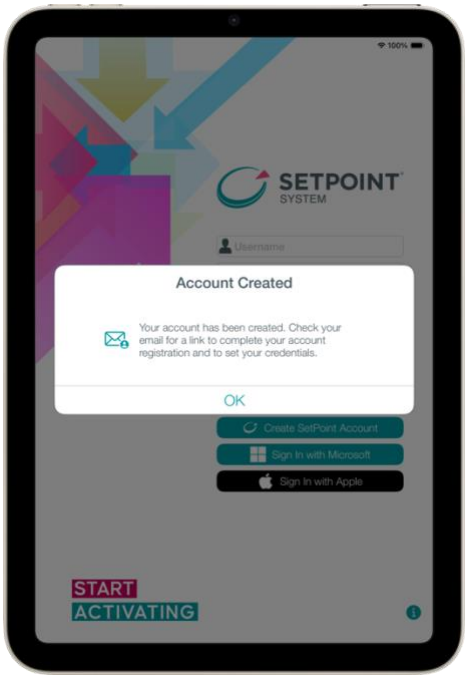


Figure 22 - Prompt Indicating Successful Account Creation

5. An email titled “Set a SetPoint Medical Password” will be delivered to your inbox. Setting a password or passkey for your account will also serve to verify the email address. In the email,

select “Set My Password” and follow the prompts in your browser to set your credentials. More information can be found in the **Resetting Credentials** section.

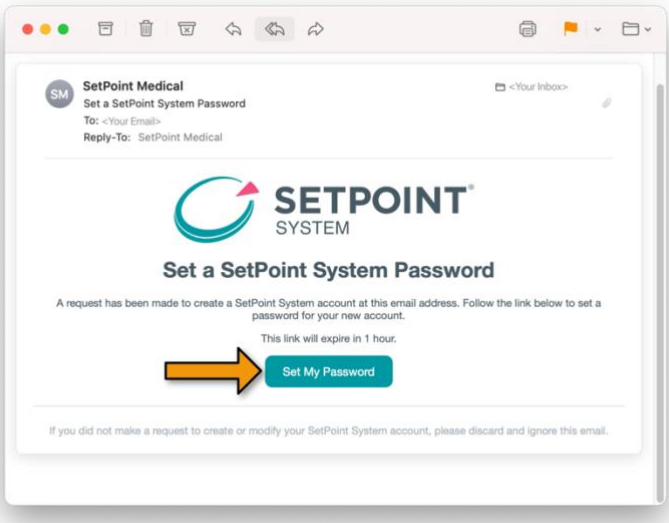


Figure 23 – The “Set My Password” Button in the Account Verification Email

6. Alternatively, to register an account managed by an alternate sign-in provider (e.g., Microsoft or Apple), simply attempt logging in with that account and follow the alternate sign-in provider’s instructions for authorizing access to the SetPoint System.

Figure 24 – Create an Account with an Alternate Sign-In Provider

7. Accounts created with alternate sign-in providers must have their associated email address verified within the SetPoint System. An email titled “Verify Your Email Address” will be delivered to your inbox. In the email, select “Verify My Account”.

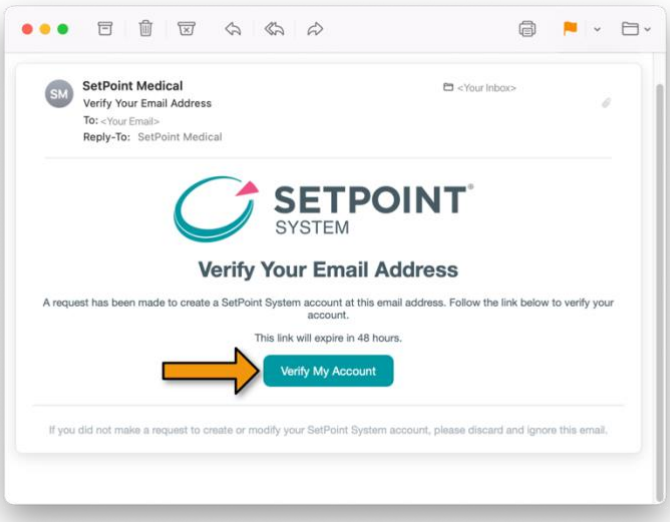


Figure 25 – The “Verify My Account” Button in the Account Verification Email

8. Once your email has been verified, you may now sign in to your account. However, you will not be able to connect to SetPoint Medical devices until your account has been approved for use after verification that you are a healthcare professional. Either your SetPoint representative or an existing user at your clinic with an activated account must make a request by sending an email to programmers@setpointmedical.com. You will receive a confirmation email at the specified address when your account is activated.

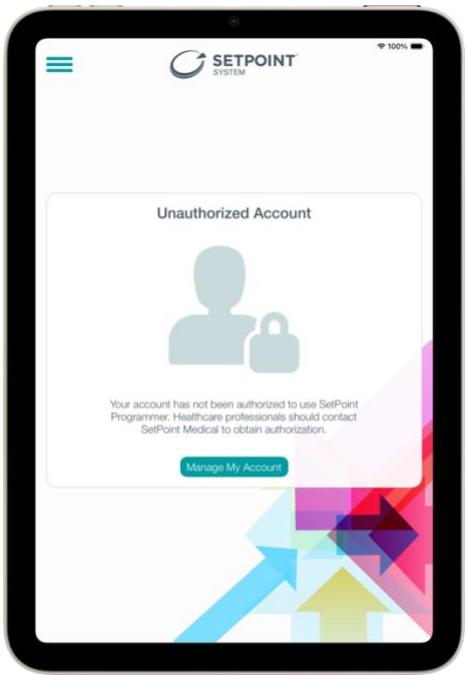


Figure 26 - Accounts have limited access to Programmer until confirmed as healthcare professionals.

Signing In and Controlling Your Account

Signing In

1. To sign in with email and password credentials, enter your username and password in the fields provided and press “Sign in with Email”. Checking “Remember My Credentials” will allow you to use Apple’s Face ID®, Touch ID®, or a connected Apple Watch® to expedite future sign-ins.

Figure 27 – Sign-In with Email and Password Credentials

2. If your account has a passkey, select the “Sign In with Passkey” button and follow the on-screen prompts to sign in.

Figure 28 – Sign-In with Passkey

3. If your account was created with an alternate sign-in provider, select the provider from the list below and follow the on-screen prompts to sign in.

Figure 29 – Sign-In with an Alternate Identity Provider

4. If your account is protected with multi-factor authentication, you may be presented with a prompt asking to select your second authentication factor.

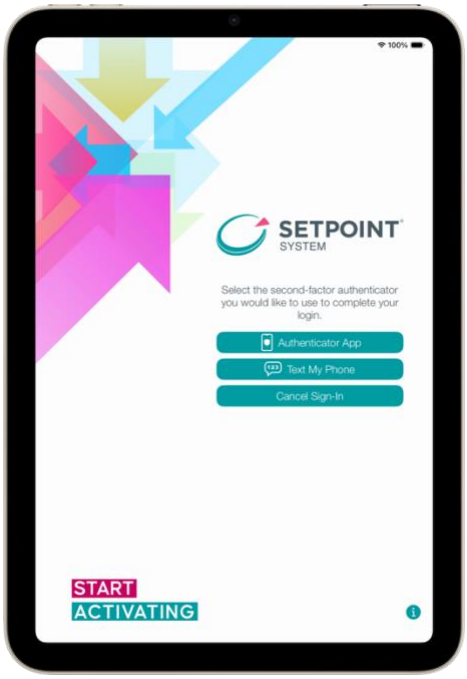


Figure 30 - Select a second authentication factor.

5. If entering a second authentication factor, enter the one-time passcode provided and press “Verify Code”.

Figure 31 - Entering a One-Time Passcode for the Second Factor

6. If logging in for the first time, an End-User License Agreement will appear. Review the license and press “Agree” to agree to the terms of the license.

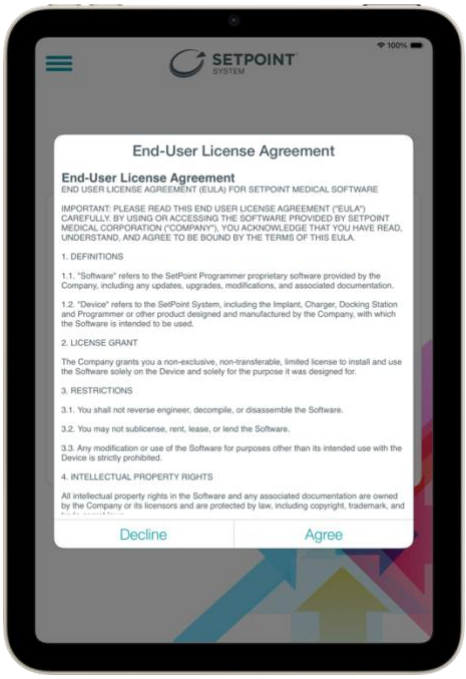


Figure 32 - End-User License Agreement

Updating User Details

Once logged in, you can modify your user details, including your name and an avatar. Press the menu icon in the upper left of the Programmer and then press “My Account”.

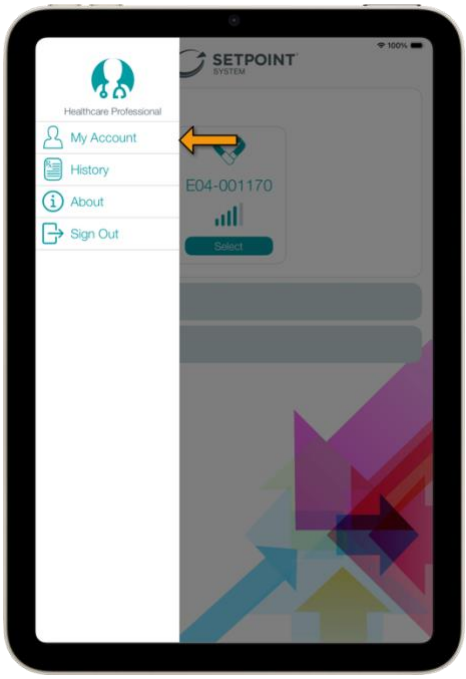


Figure 33 - Accessing the Account Manager

- To update your name in the SetPoint System, type in the Name field and press “OK”.

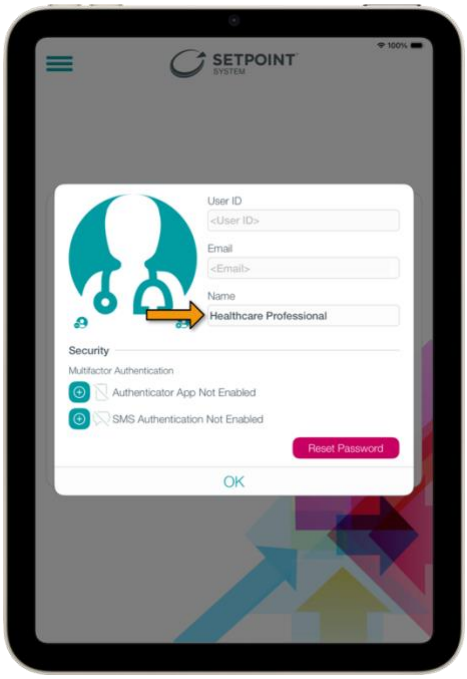


Figure 34 - Modifying Your Name

- To add an avatar image, press the “Add Avatar” button as shown below. Select a photo from the iPadOS’ built-in photo picker.

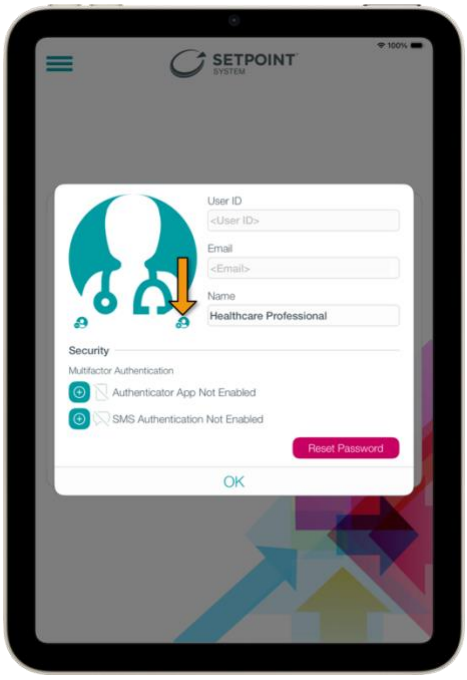


Figure 35 - Adding an Avatar

- To remove an avatar image, press the Remove Avatar button as shown below.

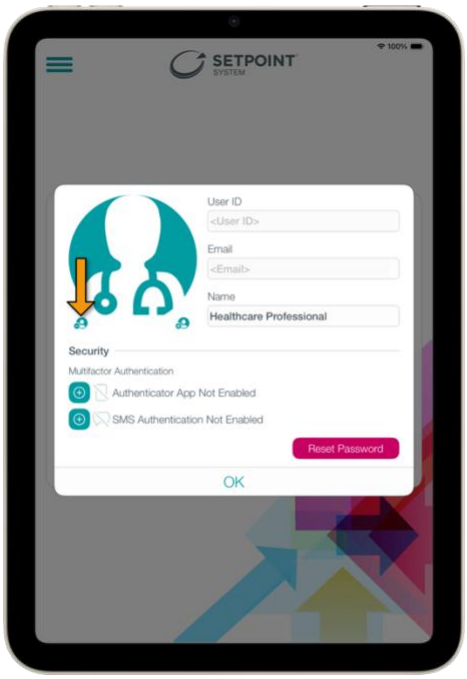


Figure 36 - Removing an Avatar

Resetting Credentials

Your credentials may be reset provided you have access to the email account with which you registered your account. SetPoint Medical does not have access to your password and SetPoint Medical personnel will never request your password.

1. From the Sign-In Screen, press “Forgot Password”.

Figure 37 - Press "Forgot Password" to begin a password reset.

2. Enter the email address with which your user account was registered.

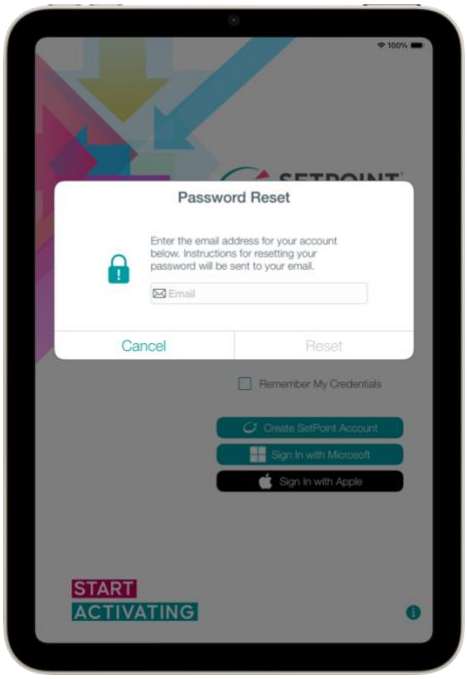


Figure 38 - Entering Your Account's Email Address for Password Reset

3. An email will be sent to the email address to reset your credentials. Open the email and select “Set My Password”.

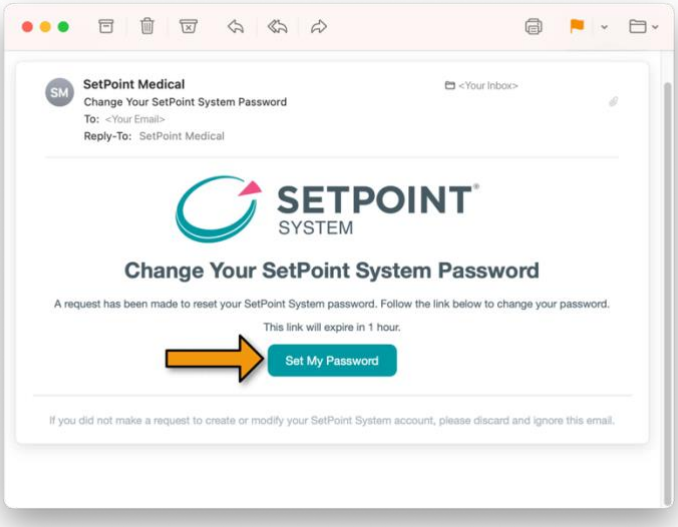


Figure 39 - The "Set My Password" Button in the Password Reset Email

4. If you have multi-factor authentication enabled, you will be required to authenticate with a second factor prior to changing your password. If prompted, select your authenticator type and enter your one-time passcode. If you have lost access to all your secondary authenticators and can no longer access your account, you will need to **contact SetPoint Medical** to reset your account’s

multifactor authentication status. Additional steps may need to be performed to verify account ownership.

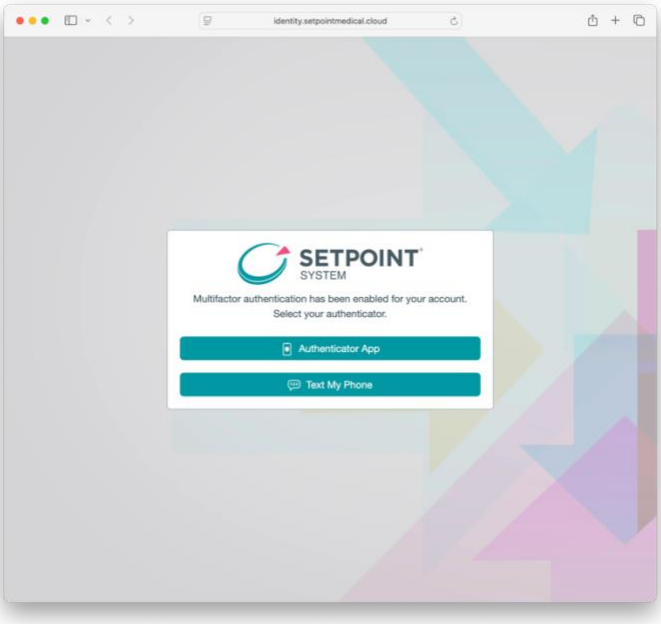


Figure 40 - Users with multi-factor authentication must authenticate prior to changing their credentials.

5. An automatically generated random passphrase, as well as an option to create a passkey, will be presented. Follow the instructions on screen to set credentials with either of these options. Alternatively, select “Choose My Own Password” to select your own password.

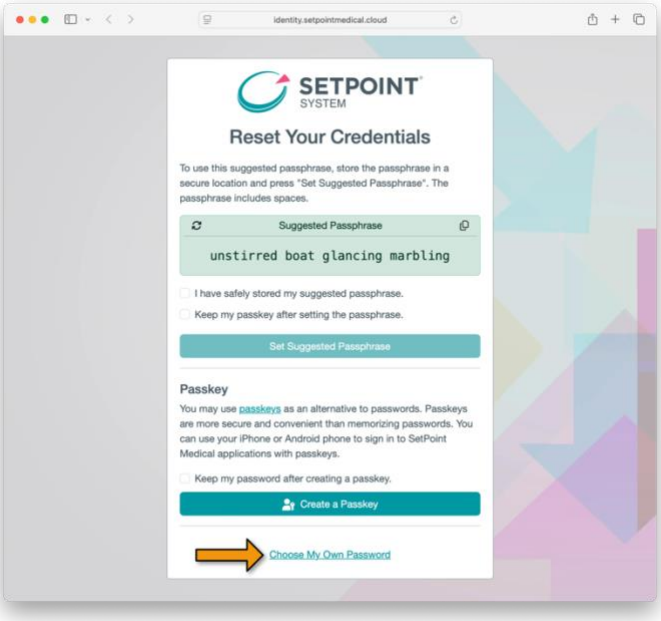


Figure 41 - Users may use a passkey, an auto-generated passphrase, or choose their own password.

6. Users that choose their own password must enter and confirm a password that has not been part of any third-party data breaches. Once a secure password has been chosen, select “Set Password”.

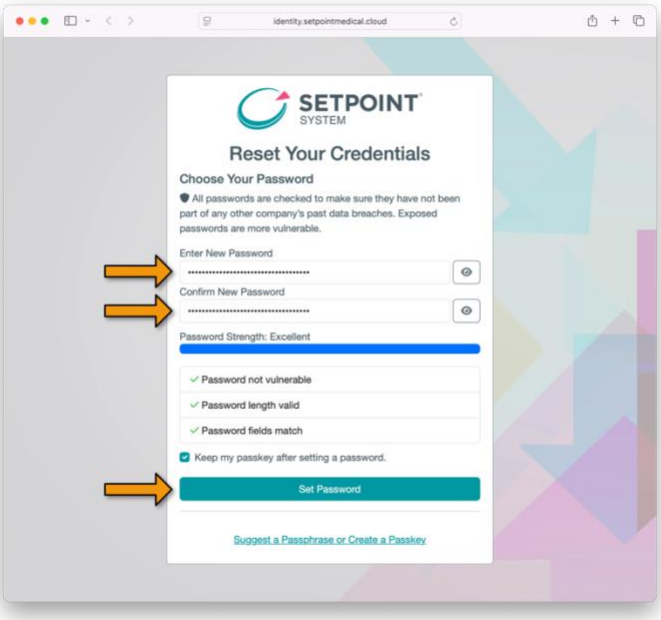


Figure 42 - User passwords may be set after it is validated against prior data breeches.

7. A display will confirm the credentials were successfully changed.

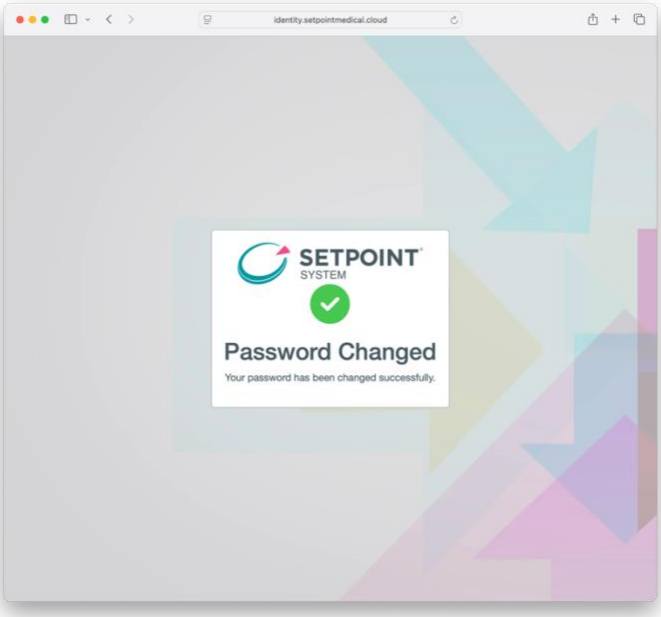


Figure 43 - Password Changed Confirmation

Managing Multi-Factor Authentication

SetPoint Medical does not require, but does recommend, that all healthcare professionals protect their account with multi-factor authentication. Programmer supports adding two forms of multi-factor authentication: having one-time passcodes sent to your cellular phone via text message and using one-time passcodes from a third-party authenticator application (e.g., Microsoft Authenticator, Google Authenticator, Authy, etc.).

Adding a Text Message Authenticator

SetPoint Medical can send text messages with one-time passcodes as a secondary authentication factor. It should be noted that latest security standards consider text messages to be a less-secure form of authentication than alternatives supported by the SetPoint System such as passkeys or authenticator applications because of frequent attacks on telephone systems.

1. After signing in to Programmer, navigate to the Account Manager as detailed in the section **Updating User Details**.
2. Press "+" next to the "SMS Authentication Not Enabled" text to turn on text message authentication.

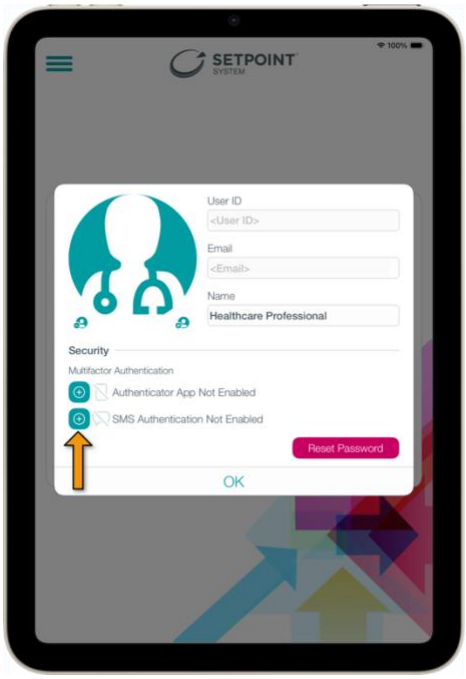


Figure 44 - Adding a Text Message Authenticator

3. Enter the phone number to which you would like to receive one-time passcodes. The phone must be capable of receiving text messages. Standard text messaging rates from your carrier may apply.

Figure 45 - Phone Number Entry

4. An initial one-time passcode will be sent to the phone number provided. Enter the code and press “Continue” to confirm your phone number.

Figure 46 - Entering the One-Time Passcode to Confirm Your Phone Number

Adding an Authenticator Application

SetPoint Medical supports the use of third-party authenticator applications as a second authentication factor. Any authenticator application or password manager that supports the Time-based One Time Password (TOTP) authenticator format will work with the SetPoint System.

1. After signing in to Programmer, navigate to the Account Manager as detailed in the section **Updating User Details**.
2. Press the "+" button next to the "Authenticator Not Enabled" text.

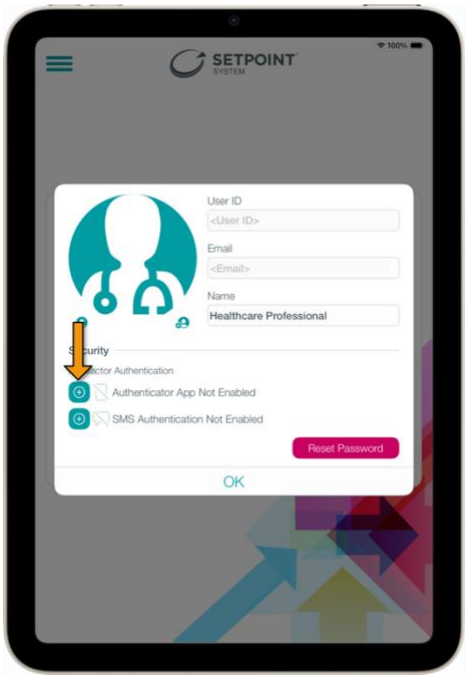


Figure 47 - Adding a Third-Party Authenticator App

3. Re-enter your credentials if prompted.
4. Using the third-party authenticator application of your choosing, scan the QR code provided and enter the one-time passcode the authenticator app provides.

Figure 48 - Confirming the Authenticator App (QR Code is Example Only)

Removing Authenticators

Once signed in, a user may remove their secondary authenticators.

1. After signing in to Programmer, navigate to the Account Manager as detailed in the section **Updating User Details**.
2. Press the button with the trash can icon next to the authenticator you wish to remove.

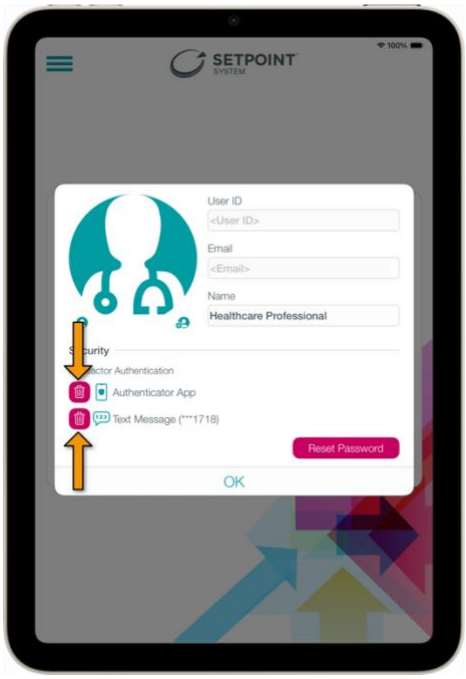


Figure 49 - Deleting Authenticators

3. Re-enter your credentials if prompted.

If you have lost access to all your secondary authenticators and can no longer access your account, you will need to **contact SetPoint Medical** to reset your account's multifactor authentication status. Additional steps may need to be performed to verify account ownership.

Programming the SetPoint System

Connecting Programmer to Charger and Implant

The patient's prescription is set by using Programmer in conjunction with the patient's Charger. Ensure the Charger is sufficiently charged prior to use by confirming a **green** LED. If the LED is **orange** the Charger is usable but should be charged soon. Refer to **Appendix A - Charger LED Status** and **Appendix B – Charger Speaker Status** for a full list of LED and speaker indications.

1. Place and close the Charger around the patient's neck.

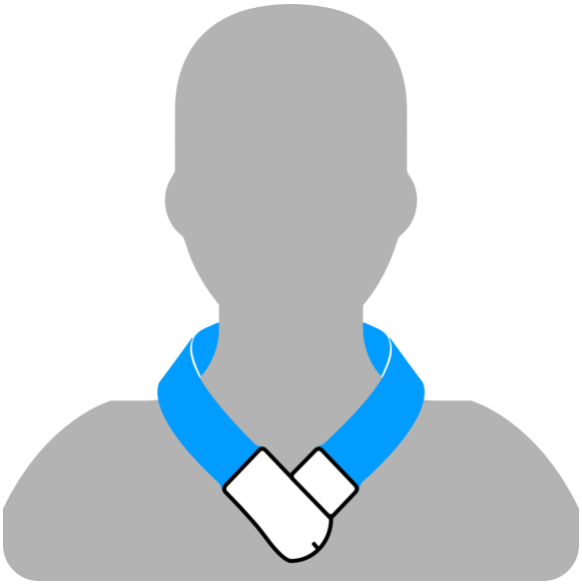


Figure 50 - A Properly Positioned Charger on a Patient

2. The Charger will automatically search for the Implant as indicated by a **pulsing white** LED.
3. Successful connection between the Charger and the Implant is indicated by **two beeps that go *up* in tone** and an **orange** or **green** LED depending on the state of the battery.
4. Launch and sign in to Programmer.
5. If prompted to allow notifications, press "Allow".

Figure 51 - Allow notifications for important programming messages.

6. If prompted to allow Bluetooth connections, press “OK”.

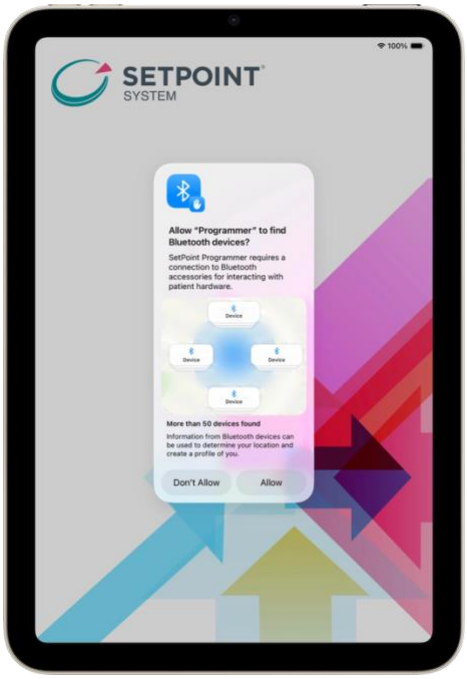


Figure 52 - Bluetooth must be enabled to connect to devices.

7. Press “Select” below the serial number printed on the back of the patient’s Charger. If prompted with a “Bluetooth Pairing Request” message, press “Pair” to confirm.

Figure 53 - The Programmer Charger Selection Screen

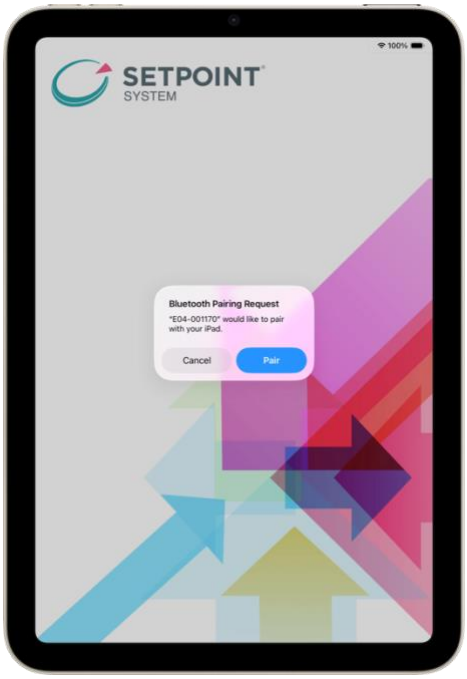


Figure 54 - Charger Bluetooth Pairing Request

8. Once the Charger LED begins **rapidly blinking blue**, tap twice on the Charger magnetic latch.

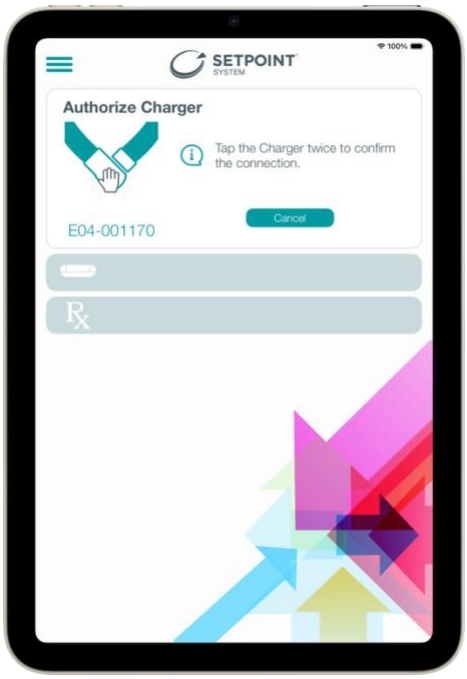


Figure 55 - Tap the Charger twice to confirm the connection to Programmer.

9. Successful connection of the Charger and Programmer is indicated by a **single long beep** on the Charger speaker and the Charger LED **periodically blinking blue**. If the Charger requires an update, it will show in the Charger Panel, press “Update” to start the process. After completion of an update, the connection to the Charger will need to be re-established.

Figure 56 - Programmer will indicate if an update is required for the Charger.

10. If an update is not required, or after completion of the update, Programmer will indicate it is connecting to an Implant.

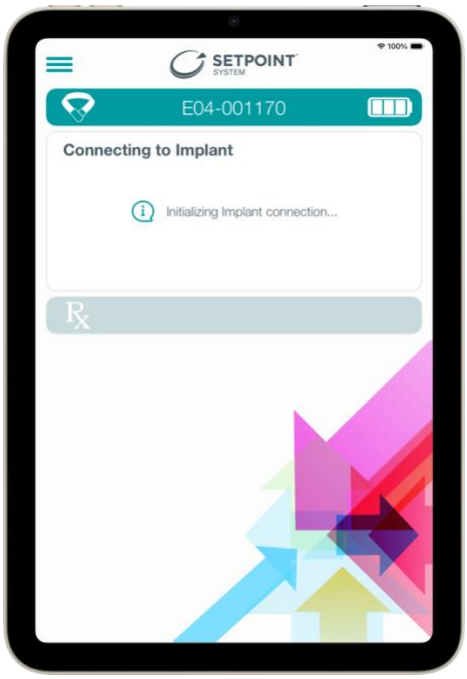


Figure 57 - Programmer will begin connecting to the Implant after connecting to the Charger.

11. Once Programmer is connected to the Implant, it will progress to the Implant Panel. If the Implant requires an update as shown in the Implant Panel, press “Update” to start the process.

Figure 58 - Programmer will indicate if an update is required for the Implant.

12. The serial number of the connected Implant will be identified by Programmer. Confirm that the Implant serial number matches the serial number in the patient’s records or on the Patient ID Card. If not, **contact SetPoint Medical** for troubleshooting.

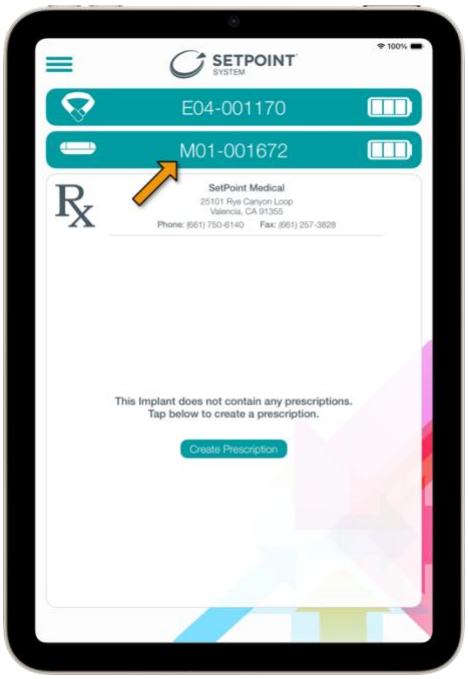


Figure 59 - The Implant serial number will be displayed in the Implant Panel of the Programmer.

13. If the Implant is not detected, the Charger LED will continue to **slowly pulse white,** and Programmer will alert you to confirm that the Charger is placed on the patient's neck and the latch is closed.

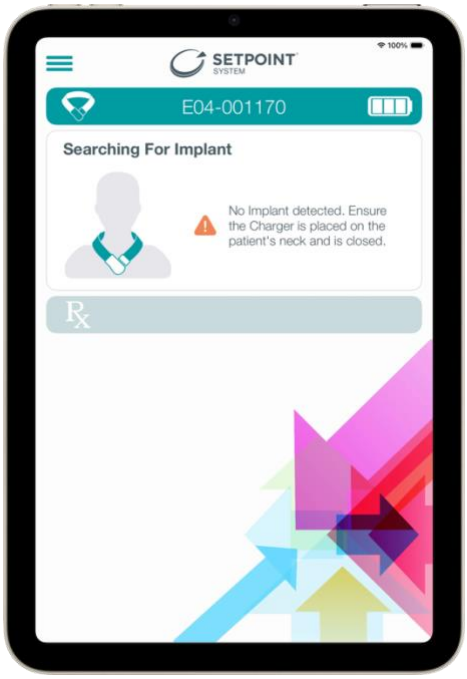


Figure 60 - If the Charger does not detect an Implant, confirm the Charger's placement on the patient and that it is latched closed.

14. If the Implant is still not detected even though the Charger is positioned properly on the patient's neck and the latch is closed, **contact SetPoint Medical** to troubleshoot.

Creating the Prescription

1. The first time the patient's Implant is programmed, it will not have a prescription. Press "Create Prescription".

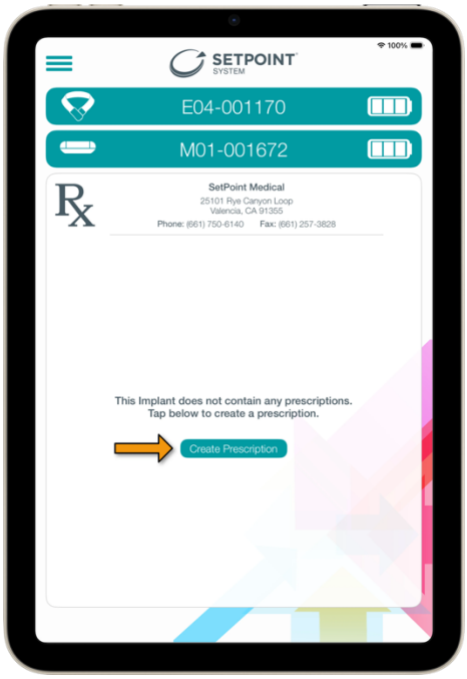


Figure 61 – Press "Create Prescription" to create the first prescription.

Adjusting Dose Strength

A default schedule for stimulation will be automatically set by Programmer when the first prescription is created. The dose duration and daily dose count will be automatically set by the Programmer and cannot be edited. Dose strength can be tested and adjusted to higher values as follows:

1. Press "Edit" to the right of "Strength".

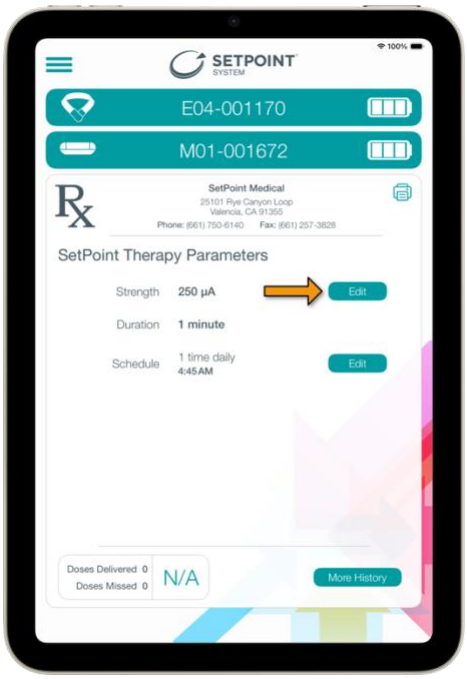


Figure 62 - Press "Edit" to the right of "Strength" to adjust the dose strength.

2. The default dose strength is 250 µA for all new prescriptions. Press “+” to increase the dose strength in increments of 50 µA or “-” to decrease the dose strength in increments of 50 µA. Programmer will limit dose strength increases to 250 µA prior to testing. The maximum dose strength is 2,500 µA, but you should stop when the maximum tolerated dose is achieved.

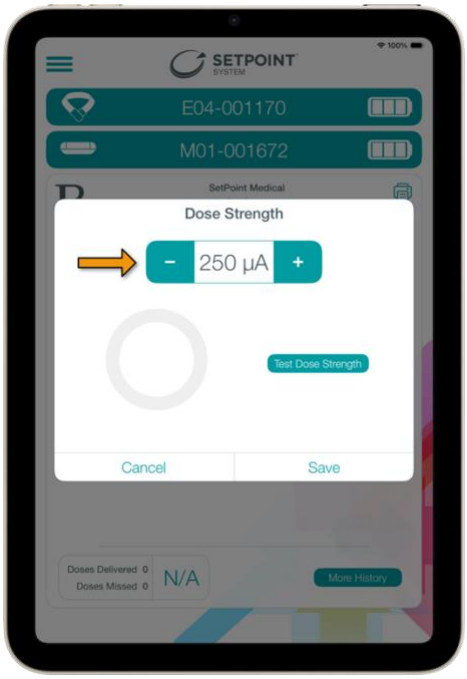


Figure 63 - Press "+" and "-" to modify dose strength.

3. Instruct the patient that testing is about to begin and that they should inform you of any discomfort. Stimulation can be stopped by pressing “Reject” in Programmer or by unlatching the Charger. If the Charger is unlatched, it can be relatched without automatically resuming stimulation.
4. Once a desired dose strength is set, press “Test Dose Strength” to initiate the test stimulation. The Charger will briefly sound a **rapid beep** pattern, and the Charger LED will **blink white** to indicate that stimulation is starting.

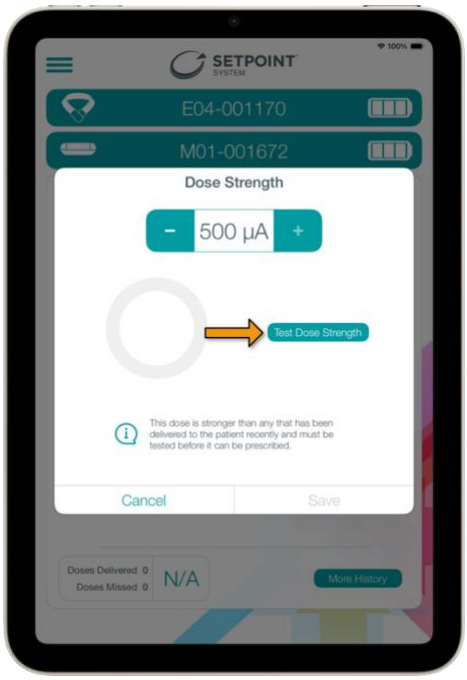


Figure 64 - Press "Test Dose Strength" to begin stimulation.

5. To be accepted, the test dose must be delivered for at least 15 seconds. If at any time the patient experiences discomfort, press “Reject” or unlatch the Charger. Note that the patient may or may not feel the test stimulation. Unless stopped, the test dose will be delivered for a total of 60 seconds.

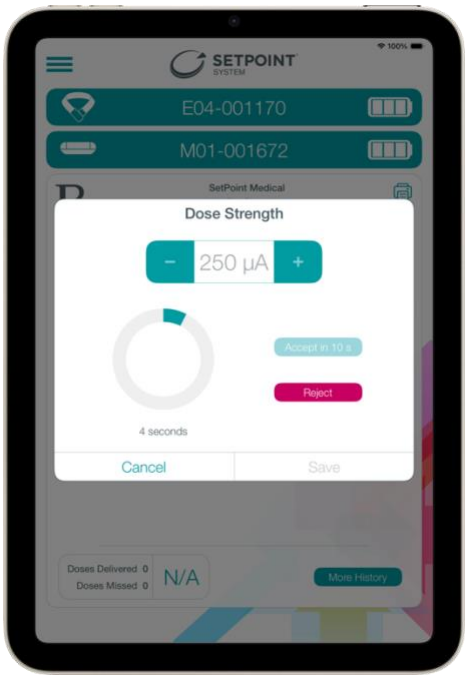


Figure 65 - A test dose may not be accepted until stimulation has occurred for at least 15 seconds. The test dose may be stopped at any time by pressing "Reject".

6. If the tested dose strength is deemed comfortable after at least 15 seconds of stimulation, press “Accept”.

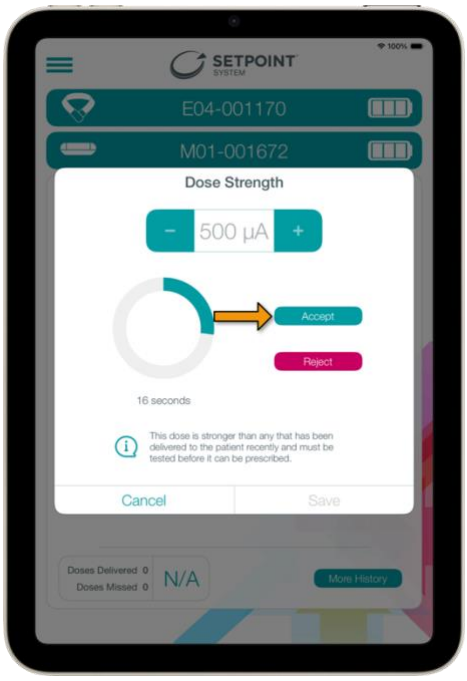


Figure 66 - The test dose may be accepted if at least 15 seconds of stimulation has elapsed, and the patient does not indicate discomfort.

7. The dose strength can be further adjusted and re-tested if needed by repeating steps 2-6.

8. Once the optimal dose strength has been determined, it can be saved as a new prescription by pressing “Save”.

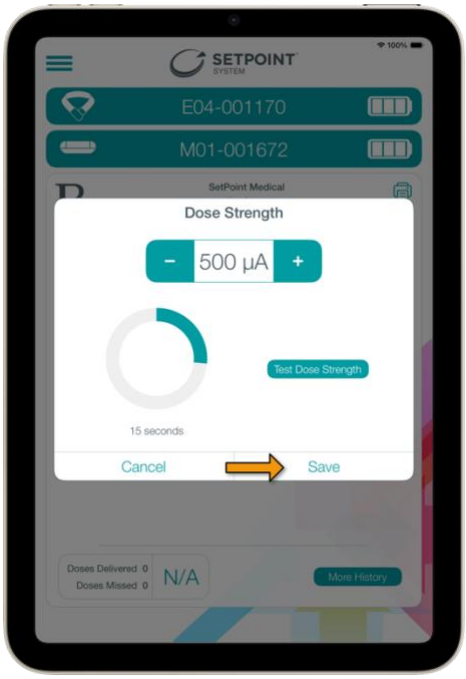


Figure 67 - Pressing "Save" will program a new prescription on the patient's Implant.

Editing Dose Schedule

The default time for stimulation will automatically be programmed for all patients. To adjust the stimulation time from the default, proceed as follows:

1. Press “Edit” to the right of “Schedule”.

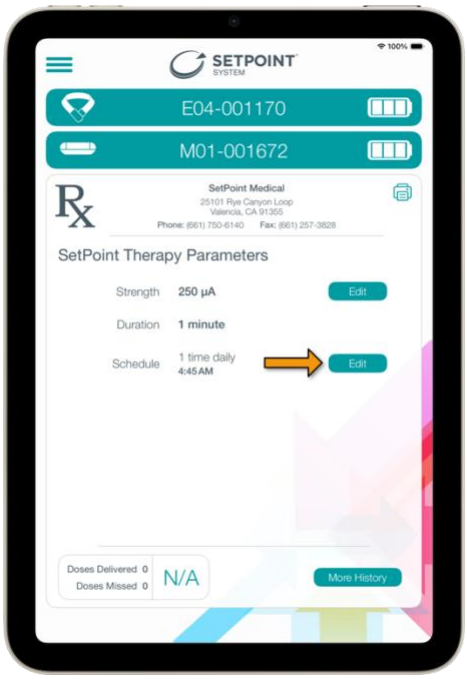


Figure 68 - Press "Edit" to the right of "Schedule" to adjust the dose schedule.

2. Move the time indicator to the desired time. Dose time may be set in increments of 15 minutes. Once the dose time has been adjusted, it can be saved to a new prescription by pressing “Save”. Note that small variations in dose delivery times are to be expected and will be corrected when the Charger is used to Charge the Implant.

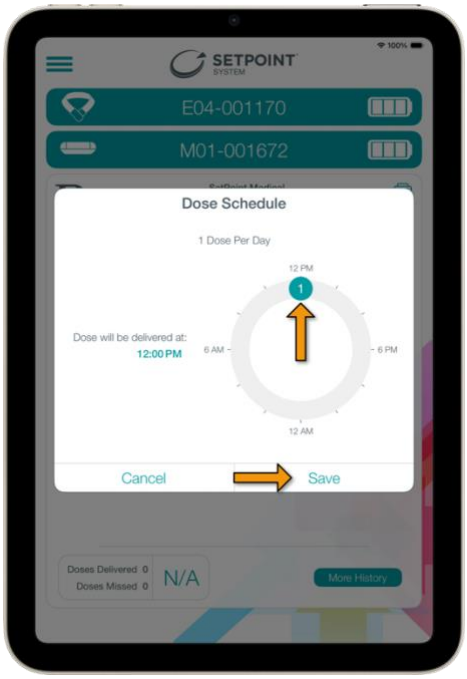


Figure 69 – Move the time indicator to modify the scheduled dose time.

Patient Prescription History

Programmer displays information about the patient's prescription history, including percentage of scheduled doses delivered. A percentage less than 100% could occur if the Implant has been suspended or if the Implant's battery has been depleted. Automatic doses will not be delivered while the Charger is being worn, either during a clinic visit or while charging at home.

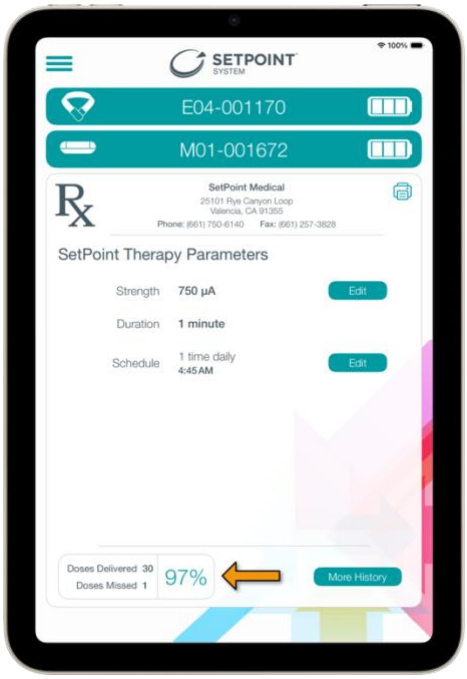


Figure 70 – History of the Current Prescription

Pressing "More History" allows you to view past prescriptions, including the dates the prescriptions were created, the dosing parameters, and the number of doses that were delivered or missed in the timeframe during which that prescription was active.

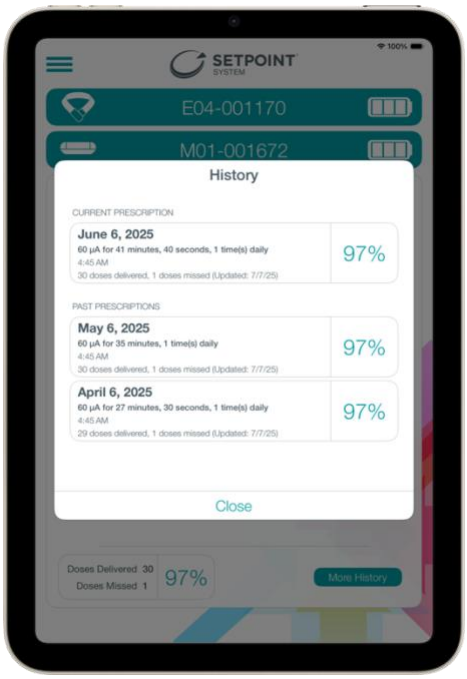


Figure 71 - Prescription History for the Connected Implant

Prescription history may be printed, if an AirPrint®-compatible printer is available on the same Wi-Fi network, by pressing the printer icon on the top-right of the Prescription Panel. For additional support on printing, refer to the iPad Owner's Manual, or check Apple support at https://support.apple.com.

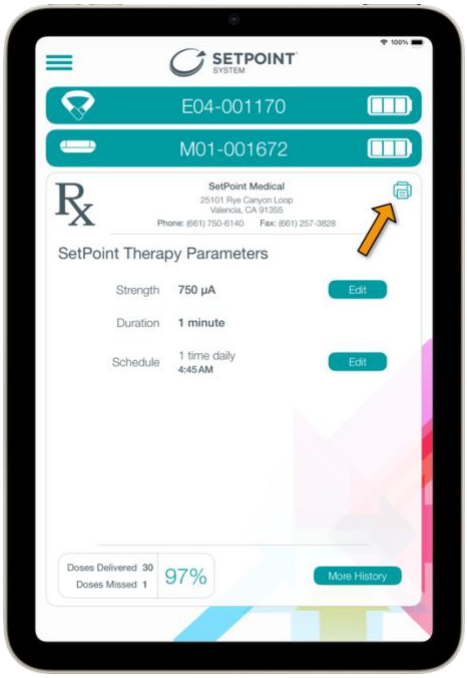


Figure 72 - Press the printer icon in the top-right corner of the Prescription Panel to print.

Prescription history can also be viewed even when the patient is not in the clinic.

1. Press the menu icon in the upper left of the Programmer and then press “History”.

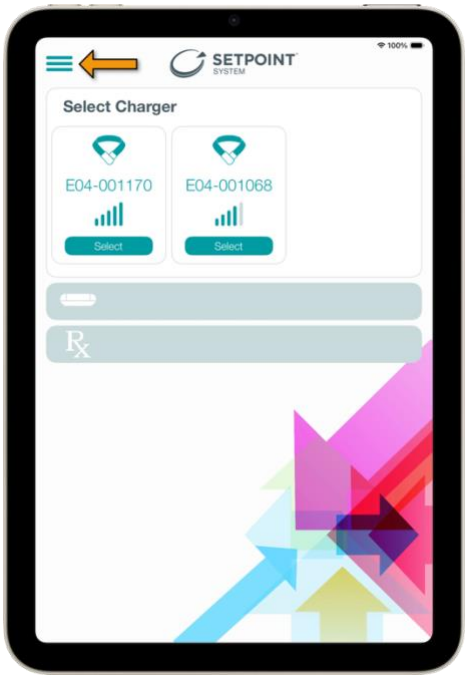


Figure 73 – Menu Icon

Figure 74 – Press "History" to retrieve prescription history.

2. A list of all the Implants that have been programmed by the clinic will appear. Press the patient’s Implant to view its prescription history.

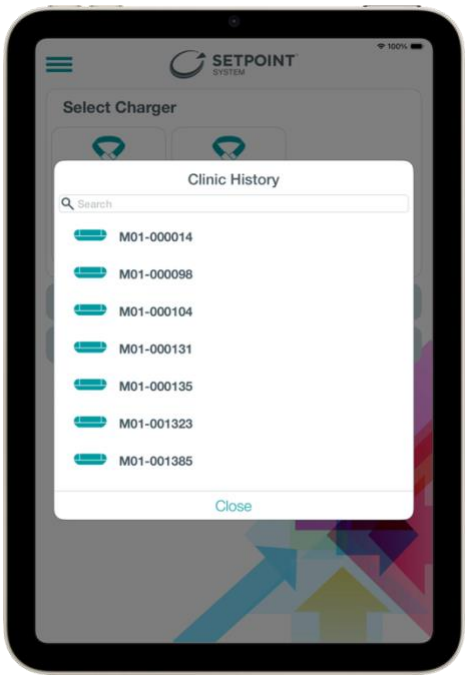


Figure 75 - All Implants Programmed by the Clinic

Suspending Therapy

Programmer can be used to temporarily suspend daily stimulation if needed. Therapy can only be resumed by a healthcare professional using Programmer.

1. Press the Implant Panel.

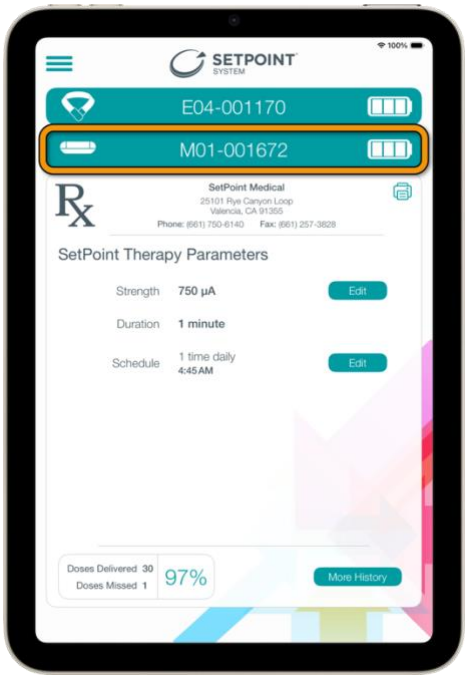


Figure 76 - Press the Implant Panel.

2. Press “Suspend Therapy”.

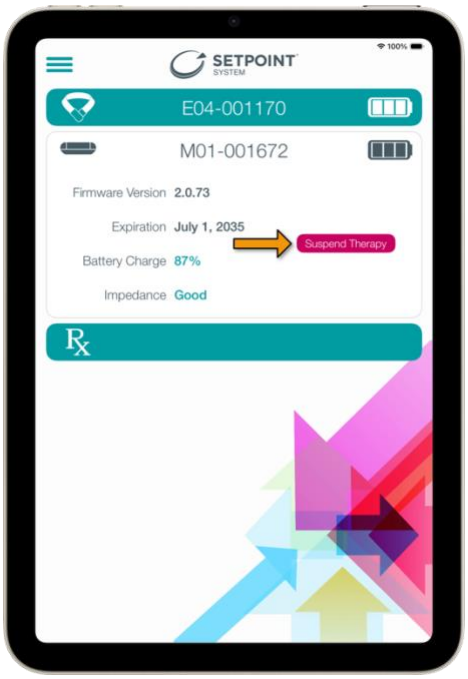


Figure 77 - Press "Suspend Therapy".

3. When prompted, press “Suspend” to confirm.

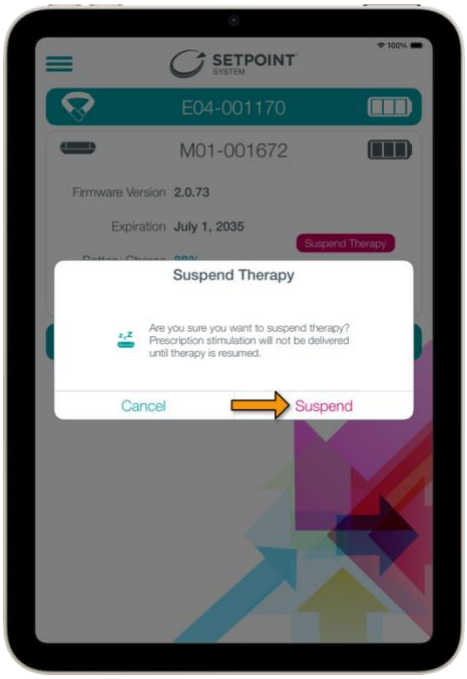


Figure 78 - Press "Suspend" to confirm therapy suspension.

4. Ensure the Charger LED shows solid **pink** to confirm therapy has been suspended.

Resuming Therapy

Programmer can be used to resume daily stimulation after temporary suspension.

1. Press the Implant Panel or the Prescription Panel.
2. Press “Resume Therapy”.

Figure 79 - From the Implant Panel, press the "Resume Therapy" button to allow the Implant to resume delivering stimulation.

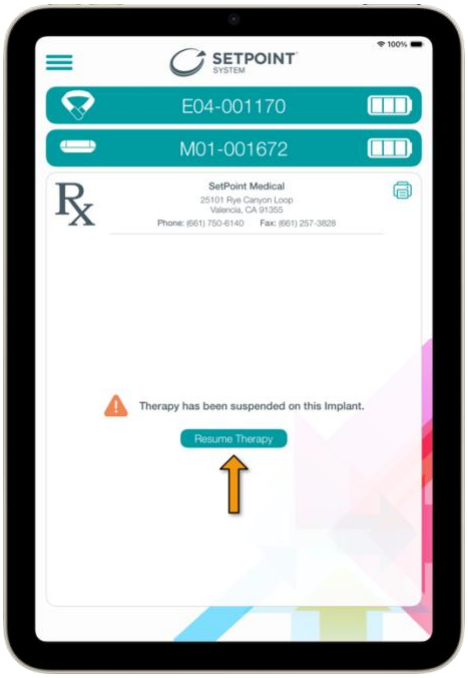


Figure 80 - From the Prescription Panel, press the "Resume Therapy" button to allow the Implant to resume delivering stimulation.

3. When prompted, press “Resume” to confirm.

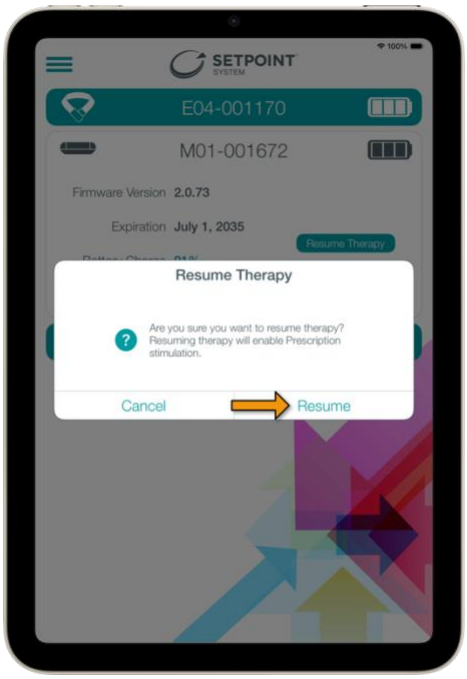


Figure 81 - Press "Resume" to confirm resumption of therapy.

4. Confirm that the prescription that was previously set, prior to suspending therapy on the Implant, is displayed in the Prescription Panel.

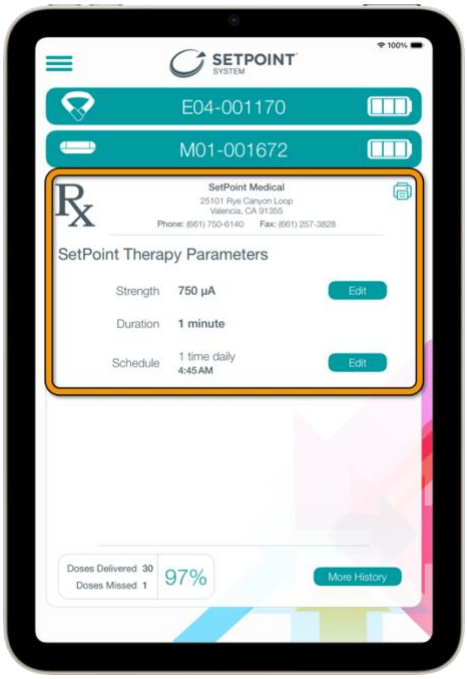


Figure 82 - Programmer will show the previously set prescription when therapy is resumed.

5. Ensure the Charger LED shows **green** or **orange** to confirm therapy has been resumed.

Implant Expiration

An Implant will have an expiration date that is appropriate for its hardware lifespan set as part of creating the first Prescription on the device. This expiration date may be viewed in the Implant Panel.

Figure 83 - An Implant Expiration More Than One Year in the Future

If the Implant's expiration date is within one calendar year of the current date, a reminder will be displayed in Programmer upon connection with the Implant. This reminder will be displayed with each connection until the Implant expires. It is important to inform the patient of the upcoming Implant expiration so that they can coordinate replacement, if desired.

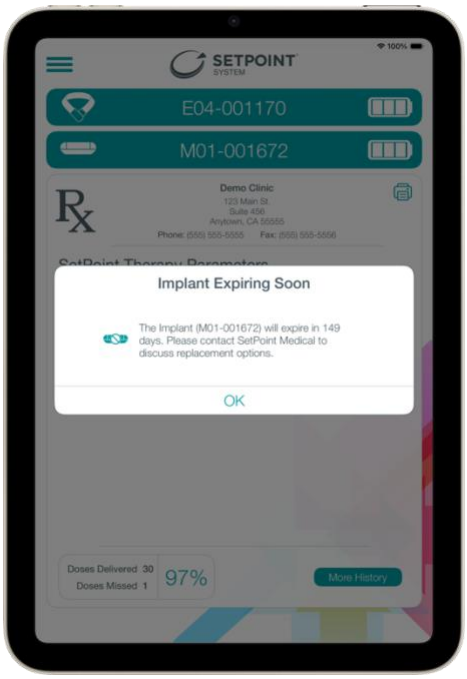


Figure 84 - An Indication that the Implant Expires Soon

Once an Implant has expired, stimulation and battery charging are no longer possible. The Prescription Panel's content will be replaced with a message that indicates this with instruction to **contact SetPoint Medical**.

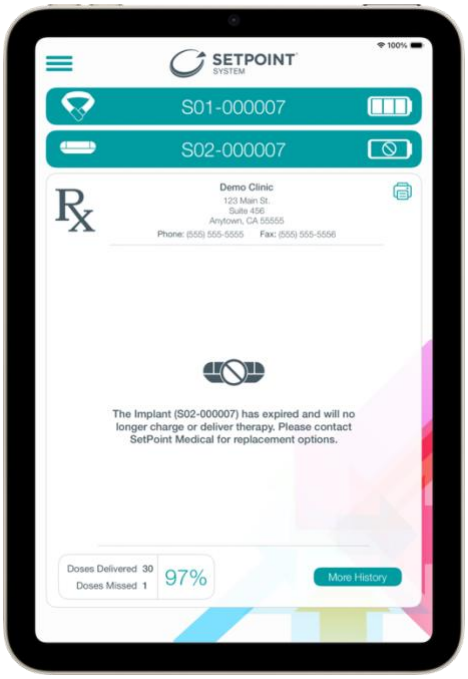


Figure 85 - The Prescription Panel's Display is Changed for an Expired Implant

Additional details of an expired Implant's status are also available in the Implant Panel. Impedance measurements and the Implant's state of charge will no longer be available. As an expired Implant is permanently in a standby state, the "Suspend Therapy" option is also unavailable.

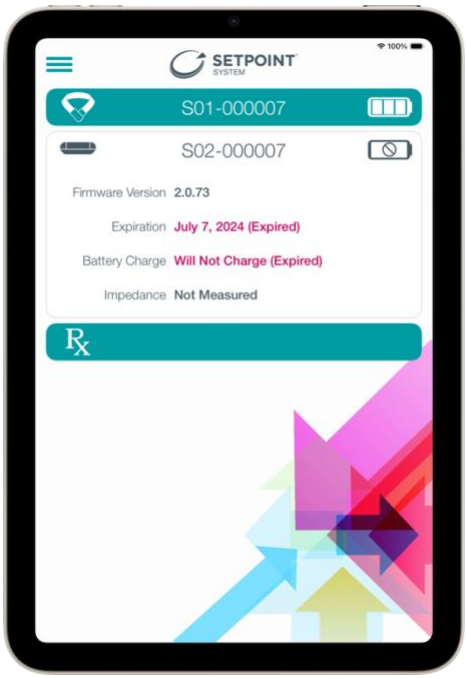
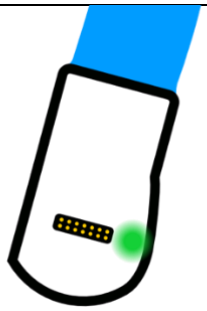
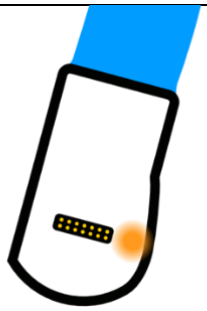
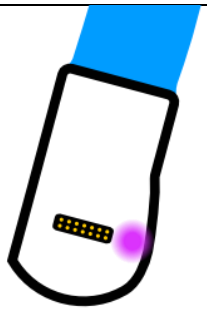


Figure 86 - An Expired Implant in the Implant Panel

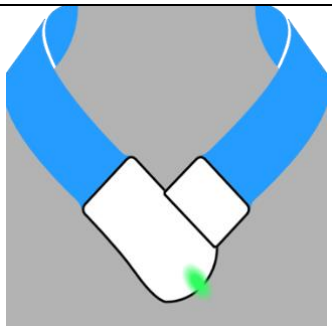
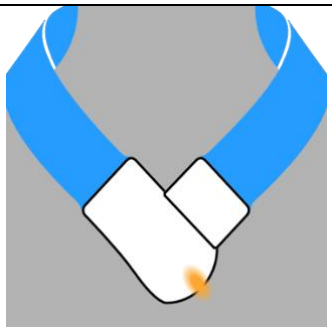
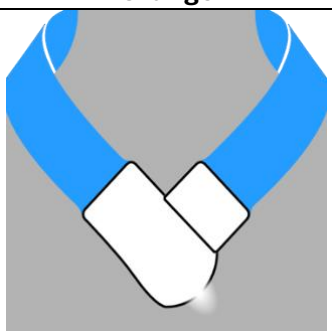
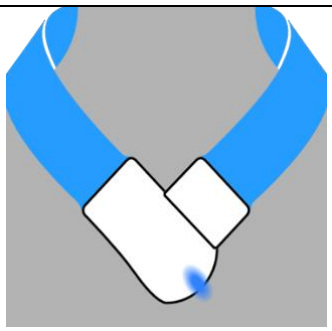
Appendix A - Charger LED Status

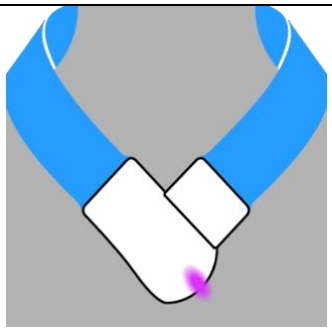
The LED on the Charger will show different things based on how it is being used.

While Unlatched

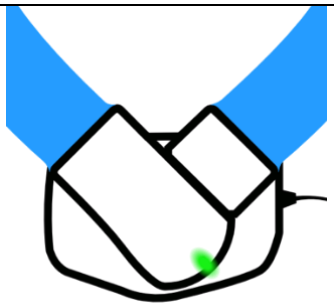
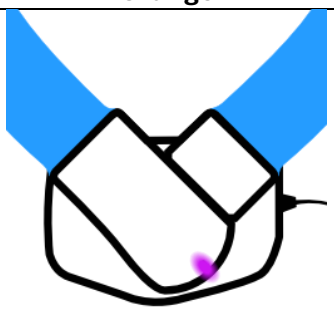
LED Color	Status
 **Green**	**Solid**: The Charger has enough charge to charge the Implant.
 **Orange**	**Solid**: The Charger does not have enough charge to charge the Implant. **Blink**: The Charger needs to be charged before it can be used, or it will turn off.
 **Pink**	**Slow Blink**: This is a warning. The Charger might be too hot. Make sure to keep it in a cool place and away from direct sunlight. **Rapid Blink**: The Charger has an error that cannot be fixed. Stop using it and **contact SetPoint Medical**.

While Being Worn

LED Color	Status
 **Green**	**Solid**: The Implant is fully charged. **Blink**: The Implant has enough charge.
 **Orange**	**Solid**: The Implant is not fully charged and has not started charging yet. **Blink**: The Implant is charging but is not full yet.
 **White**	**Slow Pulse**: The Charger is trying to connect to the Implant. **Rapid Blink**: The Implant is delivering a dose and charging will start once it is complete.
 **Blue**	**Rapid Blink**: A Bluetooth connection to the Charger is waiting for confirmation. **Periodic Blink**: There is an established Bluetooth connection to the Charger. This periodic blink will alternate with other Charger LED states.

LED Color	Status
 **Pink**	**Solid**: The Implant is suspended or beyond its 10-year service life (expired) and will not deliver doses. If expired, the battery will no longer charge. **Slow Blink**: This is a warning. • The band of the Charger might be twisted or bent. Make sure it is being worn it correctly. • The Charger might be too hot. Make sure to keep it in a cool place and away from direct sunlight. • There might be dirt or lint on the Charger's magnetic latch. Look at the **Cleaning** section in the guide for how to clean the latch. **Rapid Blink**: The Charger has an error that cannot be fixed. Stop using it and **contact SetPoint Medical**.

While on the Docking Station

LED Color	Status
 **Green**	**Solid**: The Charger is fully charged. **Blink**: The Charger has enough charge to charge the Implant.
 **Orange**	**Blink**: The Charger is charging, but not full enough to charge the Implant.
 **Pink**	**Slow Blink**: This is a warning. • The Charger may not be closed properly. The Charger cannot charge if it is not latched. • The Charger might be too hot. Make sure to keep it in a cool place and away from direct sunlight. **Rapid Blink**: The Charger has an error that cannot be fixed. Stop using it and **contact SetPoint Medical**.

Appendix B – Charger Speaker Status

Sound Pattern	Status
Two Beeps That Go *Up* in Tone	The Charger is now connected to the Implant.
Two Beeps That Go *Down* in Tone	The Charger has lost its connection with the Implant.
Single Long Beep	A BLE connection has been established between the Charger and Programmer.
Rapid Repeating Beep	The Implant has started test stimulation.
Medium Repeating Beep	The connection between the Charger and the Implant is not strong enough to start charging.
Three Beeps That Go *Up* in Tone	The Implant has started charging.
Four Beeps, Three Beeps That Go *Up* in Tone and a Fourth Beep That is a Repeat of the Last Tone	The Implant has finished charging.

Appendix C – Docking Station LED Status

LED Color	Indicator Status
 **Blue**	**Solid**: The Charger is fully charged. **Blink**: The Charger is charging.
 **Pink**	**Solid**: The Docking Station is ready for use, but the Charger is not charging.
 **Red**	**Blink**: The Docking Station has an error. • Remove the Charger from the Docking Station. • Check that there are no metal objects on or around the Docking Station. • Place the Charger on the Docking Station again. • Check that the Charger is closed. If the error continues, stop using the Docking Station, and **contact SetPoint Medical**.

Appendix D – Troubleshooting

Docking Station

Event	Cause and Resolution
The Docking Station does not show a **pink** LED when plugged in.	The Docking Station is not getting power. Check if the outlet it is plugged into is working (it is turned on, the GFI is not tripped, and the wall switch is on). If the outlet is fine but the problem continues, **contact SetPoint Medical**.
The Docking Station is **blinking red** on its LED.	This is a warning. • Check that the Charger is closed. • Check that there are no metal objects on or around the Docking Station. The Docking Station cannot charge if there are metal objects present. • The Charger and/or Docking Station might be too hot and cannot charge. Make sure to keep them in a cool place and away from direct sunlight. • Take off the Charger for a few seconds, then put it back on the Docking Station cradle. Sometimes, if it wasn't placed or seated correctly, it can stop the Charger and Docking Station from charging. If the error continues, stop using the Docking Station, and **contact SetPoint Medical**.
The Docking Station shows a **pink** LED when the Charger is placed on it.	If this persists and the LED never turns **blue**, the connection between the Charger and your Docking Station cannot be established. This could be caused by electromagnetic interference. Try changing your location, waiting until a later time, or turning off the suspected source of interference if possible. If using portable RF communications equipment, make sure they are no closer than 12 inches (30 cm) to any part of the Charger or Docking Station.

Charger

Event	Cause and Resolution
The Charger is **slowly blinking pink** on its LED.	This is a warning. • The Charger may not be closed properly. The Charger cannot charge if it is not latched. • The Charger might be too hot. Make sure to keep it in a cool place and away from direct sunlight. • The band of the Charger might be twisted or bent. Make sure to wear it correctly. • There might be dirt or lint on the Charger's latch. Look at the **Cleaning** section in the guide for how to clean the latch. If the Charger continues to **slowly blink pink**, **contact SetPoint Medical**.
The Charger is **rapidly blinking pink** on its LED.	The Charger has an error that cannot be fixed. Stop using it and **contact SetPoint Medical**.
The Charger shows a **solid pink** LED.	The Implant is suspended or beyond its 10-year service life (expired) and will not deliver doses. If expired, the battery will no longer charge. If suspended, use the Programmer to resume therapy if desired.
The Charger sounds a repeated beeping tone when worn.	The connection between the Charger and the Implant is not strong enough to start charging. The band of the Charger might be twisted or bent. Make sure it is being worn correctly. If the Charger continues the repeated beeping pattern, **contact SetPoint Medical**.
The Charger **slowly pulses white** on its LED when worn.	If this persists and the connection beeps never play, the connection between the Charger and the Implant cannot be established. This could be caused by electromagnetic interference. Try changing the patient's location, waiting until a later time, or turning off the suspected source of interference if possible. If using portable RF communications equipment, make sure they are no closer than 12 inches (30 cm) to any part of the Charger. Also check the area for other Chargers.
The Charger is **blinking** or **solid blue** on its LED, but Programmer does not display the Charger.	Programmer on a different iPad is trying to connect or is connected to the Charger. Check the area for other Programmers.

Programmer

Error Message	Cause and Resolution
Network	
Connection Error SetPoint Programmer experienced an issue with connectivity. Check your network connection and **contact SetPoint Medical** if the issue persists.	Programmer lost connection with SetPoint Medical's Cloud Infrastructure due to internet connectivity issues. Follow the procedure in the section **Troubleshooting Network Connectivity**.
Network connection unavailable.	Programmer was not able to communicate with SetPoint Medical's Cloud Infrastructure due to Internet connectivity issues. Follow the procedure in the section **Troubleshooting Network Connectivity**.
There was an error communicating with SetPoint Medical. Please check your Internet connectivity.	
Sign-In	
Your email address needs to be verified to sign in. Check your inbox for a confirmation email.	The email address for a SetPoint Medical account has not yet been verified. Follow the procedure in step 5 in the section **Creating an Account**.
Sign-in failed. Please try again.	Programmer could not connect with SetPoint Medical's Cloud Infrastructure due to internet connectivity issues. Follow the procedure in the section **Troubleshooting Network Connectivity**.
Sign-in failed. Invalid credentials.	Invalid credentials were entered. Re-enter your email, password, and multi-factor authentication, or re-authenticate with your passkey. If a credential reset is needed, follow the procedure in the section **Resetting Credentials**. **Contact SetPoint Medical** to reset multi-factor authentication, if necessary.
The attempt to sign in with your Microsoft ID failed.	Sign-in with Microsoft was not successful.
Too many text message requests have been made. Please wait or try another form of authentication.	Too many text messages were sent to the specified phone number in the last 5 minutes. Wait 5 minutes or use a different multi-factor authentication method, if available. **Contact SetPoint Medical** to reset multi-factor authentication, if necessary.
Too many one-time passcode attempts have been made. Try again in 5 minutes.	Too many incorrect multi-factor authenticator one-time passcodes were attempted during a sign-in. Wait 5 minutes before trying to sign in again. **Contact SetPoint Medical** to reset multi-factor authentication, if necessary.

Error Message	Cause and Resolution
Too many sign-in attempts have been made. Try again in 5 minutes.	Too many incorrect username and password sign-in attempts were made recently. Wait 5 minutes before trying to sign in again. See the **Resetting Credentials** section for instruction on changing your password.
Your account has not been authorized to use SetPoint Programmer. Healthcare professionals should **contact SetPoint Medical** to obtain authorization.	The account has not been approved for Programmer use by SetPoint Medical. Follow the procedure in step 8 in the section **Creating an Account**.
Your password must be changed. Check your email for instructions on changing your password.	Your password is no longer valid, possibly due to your password having been detected in a third-party data breach. See the **Resetting Credentials** section for instructions on changing a password.
Bluetooth	
Bluetooth has been disabled for SetPoint Programmer. Please enable Bluetooth in SetPoint Programmer settings.	Programmer access to Bluetooth is not allowed. Press "Open Settings" and then allow Programmer access to Bluetooth.
Bluetooth has been disabled on this iPad. Please enable Bluetooth in Settings.	iPadOS access to Bluetooth is not allowed. 1. Return to the home screen. 2. Open the "Settings" application. 3. Navigate to the Bluetooth Settings for iPadOS and enable Bluetooth.
"Programmer" would like to use Bluetooth for new connections You can allow new connections in Settings.	New Bluetooth connections have been turned off from Control Center. Press "Settings", and then press "Allow New Connections" to enable Bluetooth.
Turn on Bluetooth to Allow "Programmer" to Connect to Accessories	iPadOS access to Bluetooth is not allowed. Press "Settings" and then enable Bluetooth.
Charger	
Charger Authentication Error SetPoint Programmer encountered an error attempting to authenticate the Charger (E04-XXXXXX). Please **contact SetPoint Medical**.	Programmer cannot verify the authenticity of the Charger. **Contact SetPoint Medical**.

Error Message	Cause and Resolution
Charger disconnected. Make sure the Charger is charged and nearby.	Programmer has lost connection with the Charger, and the Charger is no longer available for a Bluetooth connection. Follow the procedure in the section **Troubleshooting Programmer and Charger Connection**.
Invalid Charger Use The connected Charger is designated for Engineering use, but the Implant is not. Please **contact SetPoint Medical**.	The Charger has been detected but is designated for internal SetPoint Medical use only. **Contact SetPoint Medical**.
Unregistered Charger The selected Charger (E04-XXXXXX) has not been registered with SetPoint Medical and was disconnected. Please **contact SetPoint Medical**.	The Charger needs to be registered in the SetPoint Medical database prior to use. **Contact SetPoint Medical**.
Implant	
Implant Authentication Error SetPoint Programmer encountered an error attempting to authenticate the Implant (M01-XXXXXX). Please **contact SetPoint Medical**.	Programmer cannot verify the authenticity of the Implant. **Contact SetPoint Medical**.
Prescription Delivery Not Confirmed The last Prescription for Implant M01-XXXXXX may not have been programmed. Please ensure the Prescription was programmed.	The Implant may have been disconnected before the prescription was written. Reconnect to the Implant to allow the prescription to be written. If the latest prescription is not shown, rerun test doses as needed and save the prescription.
This Implant (M01-XXXXXX) has not yet been enrolled in a study. Please **contact SetPoint Medical**.	The Implant is designated to participate in a study but has not been assigned to a study cohort. **Contact SetPoint Medical**.
This Implant (M01-XXXXXX) has not been registered with SetPoint Medical. Please **contact SetPoint Medical**.	The Implant needs to be registered in the SetPoint Medical database prior to use. **Contact SetPoint Medical**.

Error Message	Cause and Resolution
The patient's prescription is currently being delivered. Connection will continue when the dose is finished.	The Implant has been detected, but the automatic dose is being delivered. Please wait for stimulation to complete and the connection will be resumed.
The Implant (M01-XXXXXX) has expired and will no longer charge or deliver therapy. Please **contact SetPoint Medical** for replacement options.	The Implant is beyond its 10-year service life (expired) and will not deliver doses and the battery will no longer charge. **Contact SetPoint Medical**.
Therapy Suspend/Resume Not Confirmed The request to suspend/resume therapy for Implant M01-XXXXXX was not confirmed. Please ensure the therapy status is correct.	The Implant may have been disconnected before therapy was suspended or resumed. Reconnect to the Implant to allow the therapy state to be written.
Programmer	
This version of SetPoint Programmer is out-of-date and must be updated before logging in. Please **contact SetPoint Medical** for assistance.	An updated version of the Programmer application has been released. Upgrade to the latest version to proceed. For additional support on updating, refer to the iPad Owner's Manual, or check Apple support at https://support.apple.com.

Troubleshooting Network Connectivity

1. Retry the activity in case there was a temporary interruption in internet connectivity.
2. Ensure Wi-Fi/cellular service is connected. For additional support on network connectivity, refer to the iPad Owner's Manual, or check Apple support at https://support.apple.com.
3. Open Safari and navigate to https://setpointmedical.com/.
    a. If you can connect to the website, work with your IT department to configure the network to allow Programmer to access SetPoint Medical. Please refer to the **SetPoint IT Configuration Guide**.
    b. If you cannot connect to the website, restart the iPad. If the issue persists, **contact your IT department** to troubleshoot general network issues.

Troubleshooting Programmer and Charger Connection

1. Ensure the Charger is on by tapping the magnetic latch and observing the LED. If the LED does not illuminate, place it on the Docking Station to wake it up.
2. If the Charger LED is **blinking blue**, but the Charger is not connected in Programmer, this indicates it is connected to another Programmer. Determine which Programmer is connected and instruct them to disconnect from the Charger.
3. If connection issues to the Charger persist, **contact SetPoint Medical** for further troubleshooting.

Appendix E – Explanation of Symbols Used on Packaging and Devices

Symbol	Title	Reference	Description
21 CFR 801.109: Prescription Devices			
Rx Only	Prescription Only	(b) (1)	Caution: Federal law restricts this device to sale by or on the order of a physician
47 CFR 2.1074: Identification			
FC	FCC Declaration of Conformity	(b)	The product complies with the applicable FCC requirements
ASTM F2503			
MR	Magnetic Resonance (MR) Conditional	Fig. 5	An item with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields and the radiofrequency fields
MR	Magnetic Resonance (MR) Unsafe	Fig. 9	An item which poses unacceptable risks to the patient, medical staff or other persons within the MR environment
WEEE Directive 2012/19/EU			
	Symbol for the marking of EEE	Annex IX	Separate collection for electrical and electronic equipment
Electrical Appliances and Materials Safety Act			
	TÜV SÜD PSE Diamond Mark	N/A	Tested and certified in accordance with applicable Japanese electrical safety and performance standards for Specified Electrical Appliances and Materials
IEC 60417			
	Non-ionizing Electromagnetic Radiation	5140	To indicate elevated, potentially dangerous, levels of non-ionizing radiation
	Class II Equipment	5172	To identify equipment meeting the safety requirements specified for Class II equipment according to IEC 61140
	For Indoor Use Only	5957	To identify electrical equipment designed primarily for indoor use
IEC 60529			
IP21	Degree of Protection	N/A	Protected against solid foreign objects of 0.5 in (12.5 mm) Ø and greater; Protection against vertically falling water drops.
IP22	Degree of Protection	N/A	Protected against solid foreign objects of 0.5 in (12.5 mm) Ø and greater; Protection against vertically falling water drops when enclosure is tilted up to 15°.

International Efficiency Marking Protocol for External Power Supplies			
	International Efficiency Marking Level VI	N/A	Mark indicating EPS meets the level VI requirements at both 115 V/60 Hz and 230 V/50 Hz
ISO 15223-1: 5.1. Manufacture			
	Manufacturer	5.1.1	Indicates the medical device manufacturer
	Date of Manufacture	5.1.3	Indicates the date when the medical device was manufactured
	Use-By Date	5.1.4	Indicates the date after which the medical device is not to be used
	Catalog Number	5.1.6	Indicates the manufacturer's catalog number so that the medical device can be identified
	Serial Number	5.1.7	Indicates the manufacturer's serial number so that a specific medical device can be identified
	Model Number	5.1.10	Indicates the model number or type number of a product
ISO 15223-1: 5.2. Sterility			
	Do Not Use If Package Is Damaged and Consult Instructions for Use	5.2.8	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information
ISO 15223-1: 5.3. Storage			
	Temperature Limit	5.3.7	Indicates the temperature limits to which the medical device can be safely exposed
	Humidity Limitation	5.3.8	Indicates the range of humidity to which the medical device can be safely exposed
	Atmospheric Pressure Limitation	5.3.9	Indicates the range of atmospheric pressure to which the medical device can be safely exposed
ISO 15223-1: 5.7. Others			
	Unique Device Identifier	5.7.10	Indicates a carrier that contains unique device identifier information
ISO 7010			
	Refer to Instruction manual/booklet	M002	To signify that the instruction manual/booklet must be read
	General Warning Sign	W001	To signify a general warning

UL Solutions Marks and Label Hub			
	UL Recognized Component Mark for US and Canada	N/A	Tested and certified in accordance with applicable US and Canadian electrical safety and performance standards
N/A			
	Manufacturer Part Number	N/A	Indicates the manufacturer part number of a product

Applicable Standards and Regulations

21 CFR 801 Medical Devices – Labeling

47 CFR 2 Frequency Allocations and Radio Treaty Matters: General Rules and Regulations – Equipment Authorization Procedures

ASTM F2503 – 23 Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

Directive 2012/19/EU of the European Parliament and of the Council of 4 July 2012 on waste electrical and electronic equipment (WEEE)

Electrical Appliances and Materials Safety Act Statutory Operations and Implementation Guide (ver. 4.0)

IEC 60417:2024 Graphical Symbols for use on Equipment

IEC 60529:1989/AMS2:2013/COR1:2019 Degrees of protection provided by enclosures (IP Code)

International Efficiency Marking Protocol for External Power Supplies Version 3.0, September 2013

ISO 15223-1:2021 Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements

ISO 7010:2019 Graphical symbols – Safety colors and safety signs – Registered safety signs

Appendix F – SetPoint System Technical Description

Implant

Power Source

The Implant is internally powered by a rechargeable battery.

Characteristic	Value
Type	Secondary (Rechargeable)
Chemistry	Lithium-ion (Li-ion)
Form Factor	Cylindrical
Voltage	4.0 V (Nominal)
Capacity	3.0 mAh
Safety Features	Zero-Volt Technology

Table 3 – Implant Battery Characteristics

The rechargeable battery is rated to last for 10 years, and this duration is not impacted by any Implant settings (e.g., the strength or timing of stimulation).

Charger

⚠ **Warning:** Do not modify or tamper with the SetPoint Charger. If you do, it could alter its function or bypass safety features and result in harm.

Classification

Per IEC 60601-1, the Charger does not meet the definition of an Applied Part, only of an Accessible Part. Per clause 4.6, and per risk assessment, it was, however, tested to the more rigorous Applied Part requirements. The table below shows the relevant technical classifications for the Charger per IEC 60601-1 and collateral standards.

Classification	Value
Accessibility	Type BF, Applied Part
Power Source	Internally Powered
Mode of Operation	Continuous
Operating Environment	Home Healthcare
Transportability	Body-Worn
Transit Operability	Transit-Operable
Ingress Protection	IP22

Table 4 – Charger As-Tested Classifications

Per IEC 60601-1, the user is classified as a Patient only while the Charger is latched around their neck, and as an intended Operator while placing or removing the Charger around their neck or onto or from the Docking Station.

Power Source

The Charger is internally powered by a non-replaceable, rechargeable battery.

Characteristic	Value
Type	Secondary (Rechargeable)
Chemistry	Lithium-ion (Li-ion)
Form Factor	Pouch
Voltage	3.7 V (Nominal)
Capacity	1.0 Ah
Safety Features	Over Charge, Over Discharge, and Over Current Detection

Table 5 – Charger Battery Characteristics

On a full charge, the rechargeable battery can power the Charger for 20 to 60 minutes depending on the placement of the Charger around the neck and how optimally it is communicating with the Implant. The rechargeable battery is rated to last for 5 years, and this duration is not impacted by how the Charger is used.

Radios

The Charger contains a Bluetooth Low Energy (BLE) radio receiver that receives RF electromagnetic energy in the frequency range 2.400 GHz to 2.4835 GHz. The Charger also contains an additional inductive radio that transmits electromagnetic energy. The radio specifications are as follows:

Characteristic	Value	
	BLE Radio	Inductive Radio
Frequency Range	2.400 GHz – 2.4835 GHz	127.6 kHz – 134.4 kHz
Modulation Type	GFSK, 1Mbps	AM 2400 bps
EIRP	2.5 mW (+4 dBm)	Not Defined, Total Power ≤ 6 W

Table 6 - Radio Transmit Details

Product Markings

All Charger product markings are contained on the Charger label shown below (artwork shown is for reference only).

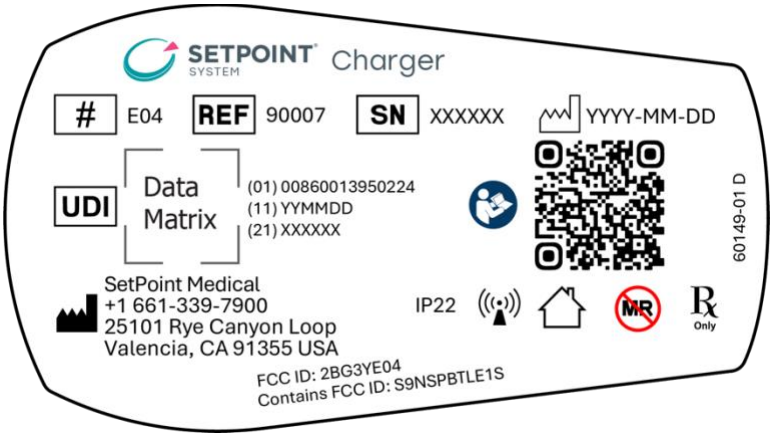


Figure 87 – Charger Label

Docking Station

⚠ **Warning:** Do not modify or tamper with the SetPoint Docking Station. If you do, it could alter its function or bypass safety features and result in harm.

Classification

The table below shows the relevant technical classifications for the Docking Station per IEC 60601-1 and collateral standards.

Classification	Value
Accessibility	Accessible Part
Power Source	Externally Powered Class II
Mode of Operation	Continuous
Operating Environment	Home Healthcare
Transportability	Portable
Transit Operability	Non-Transit-Operable
Ingress Protection	IP21

Table 7 – Docking Station Classifications

Per IEC 60601-1, the user is classified as an intended Operator while placing or removing the Charger onto or from the Docking Station.

Power Source

The Docking Station is externally powered through a power supply cord to a power supply with a mains-plug that can be removed from the mains socket-outlet to provide supply mains isolation. This non-detachable power supply cord is not replaceable.

Characteristic	Value
Input Type	AC
Input Voltage	100-240 VAC
Input Frequency	50-60 Hz
Input Max Current	1.0-0.5 A
Output Type	DC
Output Voltage	5 V
Output Max Current	2.4 A

Table 8 – Docking Station Power Supply Performance Characteristics

Product Markings

All Docking Station product markings are contained on the Docking Station and power supply labels shown below (artwork shown is for reference only).

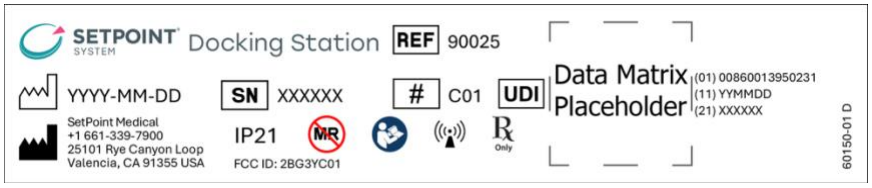


Figure 88 – Docking Station Label

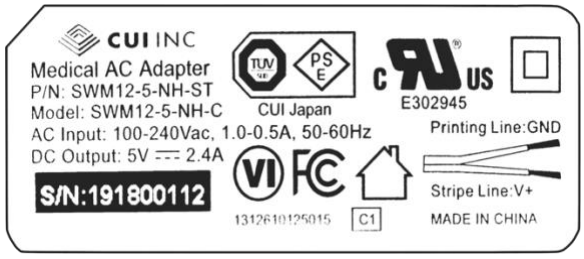


Figure 89 – Docking Station Power Supply Label

Charger and Docking Station

Emissions and Immunity Testing

The Charger and Docking Station are classified as CISPR 11 Class B Group 2 emitters. Both devices were tested with immunity test levels for use in a home healthcare environment. They were found to comply with the following immunity test standards at the specified test levels:

IEC 61000-4-2 – Charger and Docking Station Electrostatic Discharge

Device	Contact Discharge (± kV)	Air Discharge (± kV)
Charger	8	2, 4, 8, 15
Docking Station	N/A	

Table 9 - IEC 61000-4-2 Test Details

IEC 61000-4-3 – Charger and Docking Station RF EM Fields and Proximity Fields from RF Wireless Communications Equipment

- Radiated RF EM Field Exposures: 10 V/m from 80 MHz – 2.7 GHz w/80% Amplitude Modulation @1 kHz
- Proximity Field Exposures:

Test Frequency (MHz)	Modulation	Immunity Test Level (V/m)
385	Pulse, 18 Hz	27
450	Pulse, 18 Hz	28
710, 745, 780	Pulse, 217 Hz	9
810, 870, 930	Pulse, 18 Hz	28
1720, 1845, 1970, 2450	Pulse, 217 Hz	28
5240, 5500, 5785	Pulse, 217 Hz	9

Table 10 - IEC 61000-4-3 Test Details (Pulse = 50% Square Wave Duty Cycle)

IEC 61000-4-4 – Docking Station EFT/Burst

- ± 2 kV @100 kHz Repetition Frequency

IEC 61000-4-5 – Docking Station Line to Line Surge

- ± 0.5 kV and ± 1 kV

IEC 61000-4-6 – Docking Station Conducted Disturbances

- 3 V_{rms} from 150 kHz – 80 MHz

- 6 V_{rms} from 150 kHz – 80 MHz for ISM and Amateur Radio Bands w/80% Amplitude Modulation @1 kHz

IEC 61000-4-8 – Charger and Docking Station Rated Power Frequency Magnetic Field

- 30 A/m @60 Hz

IEC 61000-4-11 – Docking Station Voltage Dip and Interruption

- 100 VAC and 240 VAC @60 Hz

Voltage Level	Duration (cycles)	Phase Angle
0% of U_t	0.5	0°, 45°, 90°, 135°, 180°, 225°, 270°, 315°
0% of U_t	1	0°
70% of U_t	30	0°
0% of 120 V	300	0°

Table 11 - IEC 61000-4-11 Test Details (U_t = 100 V or 240 V)

IEC 61000-4-39 – Charger and Docking Station Proximity Magnetic Field

Test Frequency	Modulation	Immunity Test Level (/m)
30 kHz	CW	8
134.2 kHz	Pulse, 2.1 kHz	65
13.56 MHz	Pulse, 50 kHz	7.5

Table 12 - IEC 61000-4-39 Test Details (Pulse = 50% Square Wave Duty Cycle)

FCC Compliance

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.

Note: 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 or more of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.

- Connect the equipment to 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.

Changes or modifications not expressly approved by SetPoint Medical could void your authority to operate the equipment.

To maintain compliance with the FCC's RF exposure guidelines, the Docking Station should be installed and operated with a minimum distance of 8 in (20 cm) between it and your body.

Appendix G – Clinical Studies Summary

The SetPoint System has been evaluated in two U.S. clinical studies with a total of 256 implanted patients. The Pilot study (SPM-008) enrolled 14 multi-drug refractory RA patients to assess the safety and feasibility of implanting the SetPoint System, and the pivotal RESET-RA study (SPM-020) implanted 242 RA patients with inadequate response or intolerance to one (1) or more biological or targeted synthetic DMARDs to evaluate safety and efficacy of the SetPoint System.

At the time of FDA review for the SetPoint System, patients on average had been living with the Implant and receiving stimulation for longer than 1 year, with some patients, those enrolled in the Pilot study, receiving treatment for over 5 years.

This section will focus primarily on the RESET-RA study and will briefly review the Pilot study. Full analysis of the Pilot study is published in Genovese MC, Gaylis NB, Sikes D, et al. Lancet Rheumatology 2020;2(9):e527-e538.

Pilot Study (SPM-008)

Fourteen patients with multi-drug refractory RA underwent implantation with the SetPoint System in a first in human feasibility and safety study. The primary objective of the study was to determine the safety and tolerability of SetPoint System. Secondary endpoints included measurements of standard RA clinical outcomes as well as biomarker analysis of systemic inflammation.

The patients enrolled in the study were randomized to receive daily active stimulation of either 1 min QD (n=6) or 1 min QID (n=4), and non-active (sham) stimulation of 0 min QD (n=4). Efficacy outcomes presented include analysis from QD active and sham stimulation as QID dosing is not indicated for the SetPoint System. Due to the low number of patients in each group, statistically significant differences between groups were not expected, though trends that may indicate efficacy were noted.

There were no device-related adverse events noted during the conduct of the Pilot study. Treatment emergent adverse events showed no unusual adverse events during the study other than those related to the device implantation. The implantation procedure was generally well tolerated, and no perioperative infections were observed.

Six clinical adverse events associated with the implantation procedure were observed. All the observed adverse events were similar to observations documented in prior, published studies of other VNS systems or in other common surgical procedures, except for one occurrence of Horner's Syndrome, which resolved without permanent clinically significant sequelae prior to end of study. A separate incident of postoperative left vocal cord paresis occurred in this study, which is an adverse event that has been previously reported in association with vagus nerve surgery. All adverse events resolved over time and there were no permanent, clinically-significant sequalae documented.

There were no adverse, clinically significant changes noted for safety laboratory studies including CBC, electrolytes, renal function and urinalyses. There were no clinically significant changes noted for vital signs and physical examination. Cardiac safety monitoring included 12 lead ECG, rhythm strips collected during delivery of stimulation, and continuous, remote telemetry monitoring. Testing revealed no clinically significant, device associated alterations in the ECG.

Disease activity, as measured by signs and symptoms of Rheumatoid Arthritis, was evaluated using the DAS28-CRP (Disease Activity Score based on 28 joint count and C-reactive protein) as well as CDAI

(Clinical Disease Activity Index). At Week 12, 4 out of 6 patients in the QD group had changes in DAS28-CRP that exceeded the minimal clinically important difference (MCID) of -1.2 and the group mean average change in DAS28-CRP also exceeded -1.2. None of the 4 sham stimulated patients had changes in DAS28-CRP that exceeded the MCID of -1.2. Very similar results were observed when disease activity was scored using the CDAI metric, with the same number of actively stimulated QD patients exceeding the MCID of 12. None of the sham stimulated patients had changes in CDAI that exceeded the MID of -12.

An ex vivo bioassay using lipopolysaccharide (LPS)-elicited cytokine production by monocytes in culture showed that there was a substantial decrease in a subset of proinflammatory cytokines, including IL-1β, IL-6, IL-17, IL-23, and TNF-α, which are known to be relevant in RA pathophysiology at the Week 12 visit compared to Day 0 Visit. These cytokines were reduced in QD stimulated group but not in the sham stimulated group (**Figure 90**).

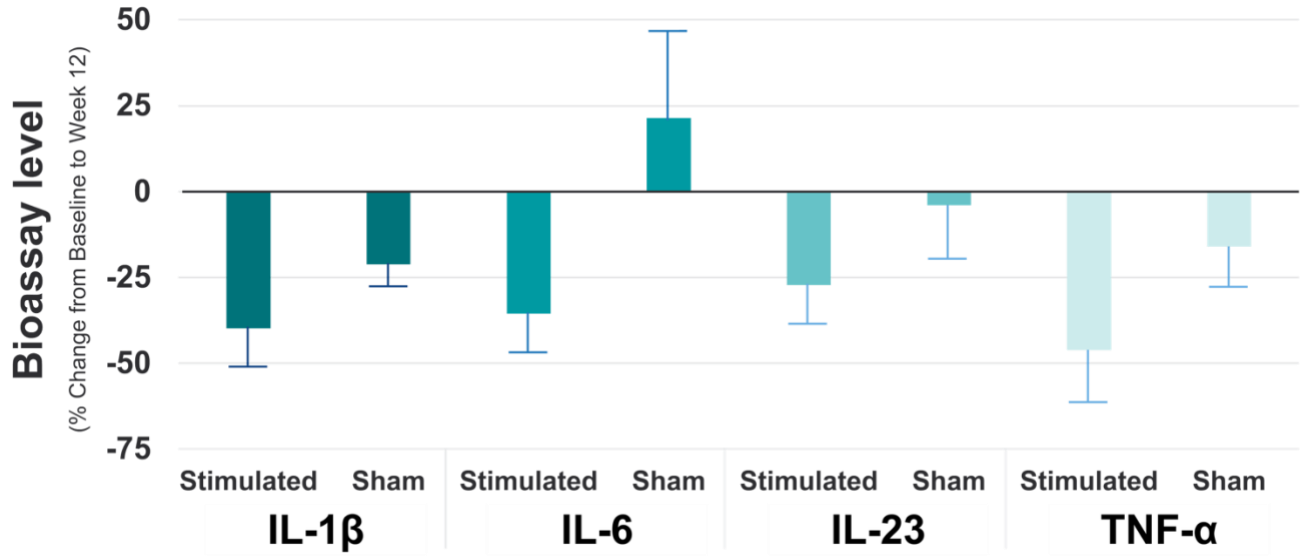


Figure 90 - Percent change from the Day 0 visit in proinflammatory cytokines levels in the TruCulture ex vivo bioassay (mean ± SME)

The primary endpoint of the Pilot study was to assess the overall safety and tolerability of the implantation surgical procedure, the device itself, and the active treatment, and, secondarily, the impact of active stimulation on RA clinical disease activity. Overall, the primary objective of the study was met as the use of the SetPoint System was well tolerated and showed initial clinical and biomarker efficacy in this group of multi-drug refractory RA patients.

RESET-RA Study (SPM-020)

RESET-RA study is a pivotal trial to assess the safety and efficacy of the SetPoint System for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response, loss of response or intolerance to at least one (1) biological or targeted synthetic DMARD (b/tsDMARD). The study enrolled 242 implanted patients across 41 study sites across the United States.

At the time of FDA review, data from the RESET-RA study was available for follow-up visits through Week 48.

Study Design

RESET-RA is a randomized, sham-controlled, double-blind, multicenter, pivotal study with 12-week follow-up for the primary efficacy endpoint, followed by one-way crossover of the control group and a 252-week open-label follow-up of all patients on active stimulation for long-term safety and effectiveness (**Figure 91**).

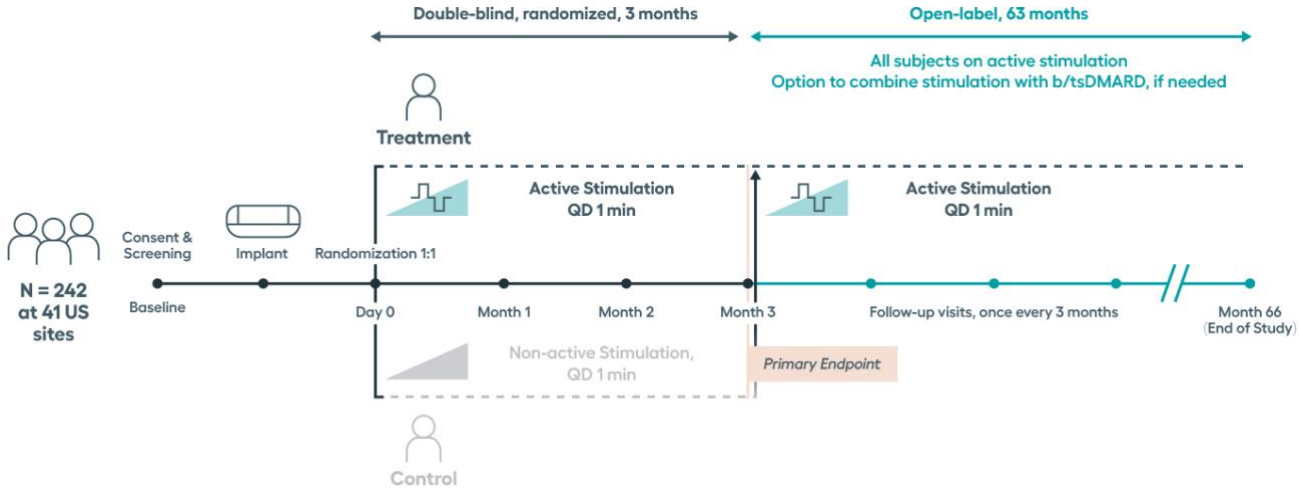


Figure 91 - RESET-RA Study Schematic

Enrollment in the RESET-RA study was limited to patients meeting eligibility criteria.

Key inclusion criteria for participation in RESET-RA included:

- 22-75 years of age at informed consent
- Moderate to severe RA, defined as at least 4/28 tender and 4/28 swollen joints
- Demonstrated inadequate response, loss of response, or intolerance to 1 or more b/tsDMARDs
- Receiving treatment with at least 1 conventional synthetic DMARD for at least 12 weeks and on a continuous non-changing dose and route of administration for at least 4 weeks prior to informed consent and able to continue the same stable dose through Week 12. Missing up to 2 doses due to COVID-19 vaccination was acceptable, except during the 4 weeks preceding informed consent.

Key exclusion criteria included:

- Current, regular use of nicotine-containing products, and lack of agreement to abstain from using nicotine-containing products throughout study participation
- Untreated or poorly controlled psychiatric illness or history of substance abuse
- Significant immunodeficiency due to underlying illness
- History of stroke or transient ischemic attack, or diagnosis of cerebrovascular fibromuscular dysplasia
- Clinically significant cardiovascular disease
- Neurological syndromes, including multiple sclerosis, Alzheimer's disease, or Parkinson's disease
- Uncontrolled fibromyalgia
- History of left or right carotid surgery
- History of unilateral or bilateral vagotomy, partial or complete splenectomy
- Recurrent vasovagal syncope episodes
- Hypersensitivity/allergy to MRI contrast agents and/or unable to perform MRI

All patients were required to remain on a stable background dose of at least 1 conventional synthetic DMARD through the primary endpoint evaluation. All patients were washed off their b/tsDMARDs prior to undergoing implantation procedure and considered enrolled once implantation is completed. Use of b/tsDMARDs from implantation procedure through Week 12 was not allowed. Addition of RA treatment, including adjunctive use of b/tsDMARD in combination with stimulation by SetPoint System, was allowed at any time after completion of Week 12 assessments if the patient experienced worsening of RA symptoms or did not experience adequate clinical improvement.

Demographics

Baseline demographics of patients in RESET-RA study, distributed by treatment and control group, are presented in **Table 13**.

	Treatment (N=122)	Control (N=120)	All (N=242)
Age (years)			
Mean (SD)	55.8 (10.3)	55.5 (10.5)	55.7 (10.4)
Median	57.0	56.5	57.0
Min, Max	25, 75	30, 75	25, 75
Gender			
Male	24 (19.7%)	10 (8.3%)	34 (14.0%)
Female	98 (80.3%)	110 (91.7%)	208 (86.0%)
Ethnicity			
Hispanic or Latino	23 (18.9%)	22 (18.3%)	45 (18.6%)
Not Hispanic or Latino	98 (80.3%)	95 (79.2%)	193 (79.8%)
Not disclosed	1 (0.8%)	3 (2.5%)	4 (1.7%)
Race [1]			
American Indian or Alaska Native	1 (0.8%)	0 (0.0%)	1 (0.4%)
Asian	4 (3.3%)	5 (4.2%)	9 (3.7%)
Black or African American	10 (8.2%)	12 (10.0%)	22 (9.1%)
Native Hawaiian or other Pacific Islander	0 (0.0%)	1 (0.8%)	1 (0.4%)
White	102 (83.6%)	93 (77.5%)	195 (80.6%)
Other	5 (4.1%)	9 (7.5%)	14 (5.8%)
BMI (kg/m^2)			
Mean (SD)	30.7 (7.3)	29.8 (6.7)	30.3 (7.0)
Median	29.6	28.7	29.2
Min, Max	18.9, 56.7	17.9, 54.1	17.9, 56.7
[1] Race reported as "Other" if more than 1 race is selected			

Table 13 - Baseline Demographics of Patients in RESET-RA Study

Medical history of prior biological and targeted synthetic DMARDs (b/tsDMARDs) is presented in **Table 14**.

	Treatment (N=122)	Control (N=120)	All (N=242)
Prior b/tsDMARDs			
Mean (SD)	2.5 (2.0)	2.7 (1.9)	2.6 (1.9)
Median	2.0	2.0	2.0
Min, Max	1.0, 12.0	1.0, 10.0	1.0, 12.0
Number of prior b/tsDMARDs			
0	0	0	0
1	52 (42.6%)	42 (35.0%)	94 (38.8%)

	Treatment (N=122)	Control (N=120)	All (N=242)
2	25 (20.5%)	28 (23.3%)	53 (21.9%)
3 or more (3+)	45 (36.9%)	50 (41.7%)	95 (39.3%)
Prior b/tsDMARD by Classification			
Anti-IL-1 agents	0 (0.0%)	4 (3.3%)	4 (1.7%)
Anti-IL-6 agents	27 (22.1%)	28 (23.3%)	55 (22.7%)
Anti-TNF agents	116 (95.1%)	109 (90.8%)	225 (93.0%)
B-cell depleting agents	13 (10.7%)	21 (17.5%)	34 (14.0%)
JAKi	25 (20.5%)	24 (20.0%)	49 (20.2%)
CTLA4-Ig	32 (26.2%)	36 (30.0%)	68 (28.1%)
Abbreviations: CTLA4-Ig, cytotoxic T-lymphocyte-associated antigen-4 immunoglobulin; IL, interleukin; JAKi, Janus kinase inhibitor; SD, standard deviation; TNF, tumor necrosis factor			

Table 14 - Baseline Prior b/tsDMARD History

Table 15 highlights the baseline disease characteristics, including components for various effectiveness outcomes such as ACR response rate, DAS28-CRP and CDAI at baseline.

	Treatment (N=122)	Control (N=120)	All (N=242)
RA duration (years)			
Mean (SD)	13.0 (10.6)	11.8 (10.4)	12.4 (10.5)
Median	10.0	8.5	9.2
Min, Max	0.1, 55.5	0.7, 51.8	0.1, 55.5
CDAI score			
Mean (SD)	36.1 (12.6)	38.2 (12.8)	37.1 (12.7)
Median	33.8	37.1	35.1
Min, Max	13.5, 73.5	16.5, 74.0	13.5, 74.0
DAS28-CRP score			
Mean (SD)	5.3 (0.91)	5.4 (0.96)	5.3 (0.93)
Median	5.2	5.3	5.3
Min, Max	3.4, 7.6	3.0, 7.9	3.0, 7.9
Serology			
Negative	56 (45.9%)	54 (45.0%)	110 (45.5%)
Positive	62 (50.8%)	66 (55.0%)	128 (52.9%)
Not Done	4 (3.3%)	0 (0.0%)	4 (1.7%)
TJC28			
Mean (SD)	14.1 (6.9)	15.0 (7.3)	14.6 (7.1)
Median	12.4	14.0	14.0
Min, Max	4.0, 28.0	4.0, 28.0	4.0, 28.0
SJC28			
Mean (SD)	9.6 (5.5)	10.5 (5.0)	10.0 (5.2)
Median	7.8	9.2	9.0
Min, Max	4.0, 28.0	4.0, 28.0	4.0, 28.0
HAQ-DI score			
Mean (SD)	1.4 (0.6)	1.3 (0.6)	1.4 (0.6)
Median	1.4	1.4	1.4
Min, Max	0.1, 2.8	0.0, 2.9	0.0, 2.9
Pain (per patient report)			
Mean (SD)	5.5 (2.0)	5.7 (2.2)	5.6 (2.1)

	Treatment (N=122)	Control (N=120)	All (N=242)
Median	5.5	6.0	6.0
Min, Max	1.0, 10.0	1.0, 10.0	1.0, 10.0
Patient Global Assessment			
Mean (SD)	6.2 (2.1)	6.0 (2.3)	6.1 (2.2)
Median	6.0	6.0	6.0
Min, Max	2.0, 10.0	1.0, 10.0	1.0, 10.0
Physician Global Assessment			
Mean (SD)	6.3 (1.9)	6.7 (1.7)	6.5 (1.8)
Median	6.3	7.0	7.0
Min, Max	1.5, 10.0	2.0, 10.0	1.5, 10.0
hsCRP (mg/L)			
Mean (SD)	8.41 (12.34)	8.01 (12.76)	8.21 (12.53)
Median	3.87	2.63	3.08
Min, Max	0.15, 69.76	0.09, 85.48	0.09, 85.48

Abbreviations: CDAI, Clinical Disease Activity Index, DAS28-CRP, Disease Activity Score using 28-joint count and C-reactive protein; Serology includes Rheumatoid Factor and/or Anti-citrullinated Protein Antibody (ACPA); TJC28, tender joint count for 28 joints; SJC28, swollen joint count for 28 joints; hsCRP, High-sensitivity C-reactive protein

Table 15 - Baseline Scores for Disease Activity and ACR Response Rate Components

Safety

Summary of safety of the SetPoint System is reported based on adverse events reporting observed during the RESET-RA study. Adverse events reported by the study doctor as related to either the implantation procedure, device or stimulation associated with the SetPoint System are summarized below.

Overall, no patients during the study experienced a life-threatening complication related to the SetPoint System, and no deaths were reported for any cause.

Summary of Adverse Events (AEs) through primary endpoint at Week 12

During the period from Screening through Week 12, non-serious AEs occurred in 13.9% of treatment and 18.3% of control patients. Most were related to the implantation procedure. The overall rate of serious adverse events (SAEs) related to the implantation procedure or SetPoint System was 1.6% based on the safety population. No events resulted in discontinuation of a patient during this period. There were no Unanticipated Adverse Device Effect (UADEs) and no deaths from Screening to Week 12. The serious adverse events related to the implantation procedure or SetPoint System during the period from implantation procedure to Week 12 are summarized in **Table 16**.

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	3 (2.5%)	1 (0.8%)
Incision site swelling [1]	1 (0.8%)	0
Vocal cord paresis [1]	1 (0.8%)	0
Dysphonia [1]	0	1 (0.8%)
Pharyngeal perforation [2]	1 (0.8%)	0

Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.
[1] Procedure-related, onset prior to randomization: incision site swelling hospitalized for evaluation that ruled out infection (resolved); vocal cord paresis with dysphagia that led to hospitalization (resolved); dysphonia deemed by investigator significant enough to impair daily activities (resolved, mild sequelae).
[2] Occurred during explant procedure, repaired intraoperatively, no hospitalization required (resolved).

Table 16 – Related, Serious AEs from Implantation Procedure to Week 12

Non-serious AEs related to the implantation procedure and/or Implant are summarized in **Table 17**. Overall, AEs related to the procedure occurred in 16% of patients. These AEs were generally mild to moderate in severity and anticipated based on the nature of the surgical intervention.

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	17 (13.9%)	22 (18.3%)
Vocal cord paresis	5 (4.1%)	6 (5%)
Dysphonia	4 (3.3%)	3 (2.5%)
Cough	1 (0.8%)	0
Diarrhea	1 (0.8%)	0
Dysphagia	1 (0.8%)	2 (1.7%)
Dyspnea	1 (0.8%)	0
Gastrointestinal complication	1 (0.8%)	0
Implant site hypoesthesia	1 (0.8%)	1 (0.8%)
Implant site inflammation	1 (0.8%)	1 (0.8%)
Implant site swelling	1 (0.8%)	2 (1.7%)
Medical device site swelling	1 (0.8%)	0
Migraine	1 (0.8%)	0
Postoperative wound infection	1 (0.8%)	0
Rash	1 (0.8%)	1 (0.8%)
Scar pain	1 (0.8%)	0
Stitch abscess	1 (0.8%)	0
Swelling	1 (0.8%)	0
Swelling of eyelid	1 (0.8%)	1 (0.8%)
Application site rash	0	2 (1.7%)
Eyelid ptosis	0	1 (0.8%)
Headache	0	1 (0.8%)
Implant site erythema	0	1 (0.8%)
Implant site pain	0	2 (1.7%)
Oropharyngeal pain	0	1 (0.8%)
Procedural pain	0	1 (0.8%)
Suture related complication	0	1 (0.8%)
Thrombophlebitis superficial	0	1 (0.8%)

Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.

Table 17 - Non-Serious Procedure or Implant Related AEs from Implant to Week 12

Stimulation therapy was well-tolerated, with all AEs reported as mild or moderate in severity (**Table 18**).

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	10 (8.2%)	0
Medical device pain	4 (3.3%)	0
Choking sensation	1 (0.8%)	0
Cough	1 (0.8%)	0
Dysgeusia	1 (0.8%)	0
Oropharyngeal pain	1 (0.8%)	0
Procedural nausea	1 (0.8%)	0
Retching	1 (0.8%)	0
Toothache	1 (0.8%)	0
Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.		

Table 18 - Stimulation Related AEs from Randomization to Week 12

There was a single event of contact dermatitis from use of the Charger. This was addressed by the patient eliminating direct contact with the Charger by wearing clothing or other fabric.

Summary of Adverse Events (AEs) in Long-Term Follow-Up

During open-label, long-term follow-up, from Week 12 until the data cut date (March 10, 2025), 5% of patients in the Treatment to Open Label (TOL) population and 4.2% in the Control to Open Label (COL) population experienced an AE related to implantation procedure or SetPoint System. None of these were serious. Most were related to stimulation, and mild or moderate in severity. Two patients discontinued treatment due to non-serious, related-AEs.

There were no related-serious AEs, Unanticipated Adverse Device Effect (UADEs) or deaths reported during Long-Term Follow-up.

There was one instance of non-serious, moderate vocal cord paresis reported after Week 12. This event is classified as related to the implantation procedure. All other AEs that occurred during long-term follow-up were related to stimulation, all were mild or moderate in severity, occurred in 5% of patients overall. (**Table 19**). These AEs were addressed by adjusting strength or time of stimulation.

MedDRA Preferred Term	TOL (N=121) n (%)	COL (N=120) n (%)
Patient with AE	6 (5%)	5 (4.2%)
Poor quality sleep	2 (1.7%)	0 (0%)
Implant site paresthesia	1 (0.8%)	0 (0%)
Medical device discomfort	1 (0.8%)	0 (0%)
*Medical device site discomfort	1 (0.8%)	0 (0%)
(exacerbation of) Trigeminal neuralgia [1]	1 (0.8%)	0 (0%)
Dysphonia	0 (0%)	1 (0.8%)
*Implant site pain	0 (0%)	1 (0.8%)
Muscle spasms	0 (0%)	1 (0.8%)
Presyncope	0 (0%)	1 (0.8%)
Temporomandibular joint syndrome	0 (0%)	1 (0.8%)
Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.		

MedDRA Preferred Term	TOL (N=121) n (%)	COL (N=120) n (%)
*Relationship to implant device was also indicated for these events [1] Exacerbation of neuralgic symptoms of trigeminal neuralgia		

Table 19 - Stimulation Related AEs during Long-Term Follow-up

Explant Summary

At the time of FDA review for the SetPoint System, the Implant was explanted in 14 of the 242 (5.8% patients). The average duration between implantation and explant among the 14 patients was 469 days, ranging from 141 to 1,364 days. No patients were explanted through Week 12 visit, and 1 Implant was explanted between Week 12 and Week 24 visits. The remainder were explanted after the Week 24 visit.

Effectiveness

The primary endpoint of the RESET-RA study was the proportion of patients achieving ACR20 response at Week 12 from baseline at day of informed consent. After Week 12, the study was open label, with one-way crossover of patients in the control group to the treatment group, with efficacy assessments repeated every 12 weeks. Patients were imputed as non-responder if rescued with steroids or b/tsDMARDs or if missing any data at Week 12 and excluded at all other time points.

ACR20 response at Week 12 showed a statistically significant difference between treatment and control groups (p-value=0.0209, 95% CI 0.6 to 23.1) (**Table 20**).

All Patients						
Group	Total	Number	ACR20 Response %	Difference from Control		
				Difference	95% CI for Difference	p-Value*
Treatment	122	43	35.2%	11.8%	0.6, 23.1	0.0209
Control	120	29	24.2%			
*p-value for all patients based on the Cochran-Mantel-Haenszel test accounting for stratification.						

Table 20 - ACR20 Response at Week 12 from Baseline by Intention-to-treat (ITT)

The evolution of ACR20 response rate through Week 48 is presented in **Table 21**. During Open-Label Follow-up, rates are reported as All Completers and Non-Augmented and show ACR20 response rates further improved and appear to be durable.

ACR20 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
Baseline	122	0.0% (0)	0.00	120	0.0% (0)	0.00	N/A	
0	122	4.1% (5)	0.02	120	10.8% (13)	0.03		
4	115	27.8% (32)	0.04	113	24.8% (28)	0.04		
8	118	33.9% (40)	0.04	113	26.5% (30)	0.04		
12	122	35.2% (43)	0.04	120	24.2% (29)	0.04		
Long-term Follow-up, All completers								
24	119	44.5% (53)	0.05	117	55.6% (65)	0.05	236	50.0% (118)
36	119	47.9% (57)	0.05	115	55.6% (64)	0.05	234	51.7% (121)
48	119	51.3% (61)	0.05	114	54.4% (62)	0.05	233	52.8% (123)
Long-term Follow-up, Non-augmented								
24	96	52.1% (50)	0.05	98	53.1% (52)	0.50	194	52.6% (102)
36	89	51.7% (46)	0.05	87	62.1% (54)	0.05	176	56.8% (100)

48	77	55.8% (43)	0.06	81	59.3% (48)	0.05	158	57.6% (91)

Note: Baseline/screening at time of consent, Day 0 (day of randomization); patient imputed as non-responder if rescued prior to Week 12, regardless of treatment assignment; patient imputed as non-responder if missing at Week 12. Non-augmented represents patients on SetPoint System monotherapy, without addition of b/tsDMARDs or high-dose steroid therapy.

Table 21 - Evolution of ACR20 Response Through Week 48

The benefits of the SetPoint Therapy may improve slowly over the first 24 weeks of treatment, especially among those who have had experience with multiple prior b/tsDMARDs. Long-term results suggest that the effects of SetPoint Therapy are significant and durable across the entire study population.

Although not statistically powered for the secondary endpoints, consistent trends in favor of treatment were seen across secondary endpoints at Week 12, with results further improved or maintained during Open-Label Follow-up reported from Week 24 through Week 48 as All Completers and Non-Augmented (**Table 22)**.

ACR20 Response from Day 0 by ITT – at Week 12					
Group	**n**	**% (n)**	**Difference from Control**		
			Difference	**95% CI for Difference**	**p-Value**
Treatment	122	31.1% (38)	8.0%	-3.1, 19.0	0.0797
Control	120	22.5% (27)			

ACR20 Response from Day 0 – in open label follow up						
Study Week	**TOL**		**COL**		**All Treated**	
	n	**% (n)**	**n**	**% (n)**	**n**	**% (n)**
Long-term Follow-up, All completers						
24	119	43.7% (52)	117	47.9% (56)	236	45.8% (108)
36	119	50.4% (60)	115	52.2% (60)	234	51.3% (120)
48	119	48.7% (58)	114	44.7% (51)	233	46.8% (109)
Long-term Follow-up, Non-augmented						
24	96	46.9% (45)	98	49.0% (48)	194	47.9% (93)
36	89	49.4% (44)	87	57.5% (50)	176	53.4% (94)
48	77	49.3% (38)	81	48.1% (39)	158	48.7% (77)

DAS28-CRP good/moderate EULAR response by ITT – at Week 12					
Group	**n**	**% (n)**	**Difference from Control**		
			Difference	**95% CI for Difference**	**p-Value**
Treatment	122	60.7% (74)	19.5%	7.3, 31.7	0.0048
Control	120	41.7% (50)			

DAS28-CRP good/moderate EULAR response – in open label follow up						
Study Week	**TOL**		**COL**		**All Treated**	
	n	**% (n)**	**n**	**% (n)**	**n**	**% (n)**
Long-term Follow-up, All completers						
24	118	66.1% (78)	117	70.1% (82)	235	68.1% (160)
36	114	73.7% (84)	107	75.7% (81)	221	74.7% (165)
48	117	72.6% (85)	111	76.6% (85)	228	74.6% (170)
Long-term Follow-up, Non-augmented						
24	95	73.7% (70)	98	70.4% (69)	193	72.0% (139)
36	85	75.3% (64)	82	78.0% (64)	167	76.6% (128)
48	75	77.3% (58)	79	77.2% (61)	154	77.3% (119)

DAS28-CRP response (MCID -1.2) by ITT – at Week 12			
Group	**n**	**% (n)**	**Difference from Control**

			Difference	95% CI for Difference	p-Value
Treatment	122	45.1% (55)	13.2%	1.1, 25.3	0.0528
Control	120	32.5% (39)			

DAS28-CRP response (MCID -1.2) – in open label follow up						
Study Week	TOL		COL		All Treated	
	n	% (n)	n	% (n)	n	% (n)
Long-term Follow-up, All completers						
24	118	53.4% (63)	117	59.8% (70)	235	56.6% (133)
36	114	58.8% (67)	107	62.6% (67)	221	60.6% (134)
48	117	62.4% (73)	111	60.4% (67)	228	61.4% (140)
Long-term Follow-up, Non-augmented						
24	95	60.0% (57)	98	62.2% (61)	193	61.1% (118)
36	85	61.2% (52)	82	64.6% (53)	167	62.9% (105)
48	75	66.7% (50)	79	63.3% (50)	154	64.9% (100)

HAQ-DI Response (MCID ≤ -0.22) by ITT – at Week 12					
Group	n	% (n)	Difference from Control		
			Difference	95% CI for Difference	p-Value
Treatment	122	45.9% (56)	9.0%	-3.3, 21.4	0.0797
Control	120	36.7% (44)			

HAQ-DI Response (MCID ≤ -0.22) – in open label follow up						
Study Week	TOL		COL		All Treated	
	n	% (n)	n	% (n)	n	% (n)
Long-term Follow-up, All completers						
24	119	53.8% (64)	117	61.5% (72)	236	57.6% (136)
36	118	57.6% (68)	115	58.3% (67)	233	57.9% (135)
48	119	55.5% (66)	113	59.3% (67)	232	57.3% (133)
Long-term Follow-up, Non-augmented						
24	96	58.3% (56)	98	63.3% (62)	194	60.8% (118)
36	89	59.5% (53)	87	58.6% (51)	176	59.1% (104)
48	77	53.2% (41)	80	61.2% (49)	157	57.3% (90)

Table 22 - Secondary Efficacy Endpoints at Week 12 and Through Week 48

Table 23 and **Table 24** present mean changes in tender and swollen joint counts from baseline of 14.6 tender joints, and 10 swollen joints (based on 28 joint count) through Week 48.

TJC Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)		
	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD
0	122	-0.4	6.14	120	-1.2	6.47	N/A		
4	116	-5.3	7.38	113	-3.5	8.35			
8	118	-6.1	7.54	113	-3.9	7.85			
12	116	-6.3	8.15	114	-4.3	9.2			
Long-term Follow-up, All completers									
24	119	-7.4	7.63	117	-7.9	9.26	236	-7.6	8.46
36	118	-7.6	7.99	114	-8.8	8.98	232	-8.2	8.50
48	119	-7.9	8.28	114	-8.0	9.12	233	-7.9	8.70
Long-term Follow-up, Non-augmented									
24	96	-8.2	7.75	98	-8.1	9.42	194	-8.14	8.61
36	88	-7.4	7.62	87	-9.9	8.94	175	-8.6	8.37
48	77	-8.3	7.82	80	-9.0	9.24	157	-8.7	8.55

Table 23 - Mean Change in Tender Joint Count for 28 Joints (TJC28) From Baseline Through Week 48

SJC Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)		
	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD
0	122	-0.7	4.53	120	-1.0	4.86	N/A		
4	116	-3.8	5.46	113	-2.8	5.8			
8	118	-4.7	5.79	113	-3.2	5.53			
12	116	-4.4	5.99	114	-3.3	5.59			
Long-term Follow-up, All completers									
24	119	-5.4	6.35	117	-5.7	5.93	236	-5.5	6.14
36	118	-5.7	6.03	114	-6.3	6.27	232	-6.0	6.14
48	119	-5.2	7.07	114	-6.5	5.88	233	-5.8	6.53
Long-term Follow-up, Non-augmented									
24	96	-5.7	6.23	98	-5.5	5.82	194	-5.6	6.02
36	88	-5.6	5.31	87	-6.7	6.19	175	-6.1	5.77
48	77	-5.9	6.14	80	-6.7	5.76	157	-6.3	5.94

Table 24 - Mean Change in Swollen Joint Count For 28 Joints (SJC28) From Baseline Through Week 48

The evolution of proportion of patients with CDAI<10 and DAS28-CRP<3.2, representing patients in low disease activity (LDA) or remission, from randomization through Week 48 is presented in **Table 25** and **Table 26**, respectively.

CDAI < 10 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
0	122	0.8% (1)	0.01	120	4.2% (5)	0.02	N/A	
4	115	18.3% (21)	0.04	113	8.0% (9)	0.03		

CDAI < 10 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
8	118	19.5% (23)	0.04	113	11.5% (13)	0.03		
12	120	23.3% (28)	0.04	119	16.0% (19)	0.03		
Long-term Follow-up, All completers								
24	119	27.7% (33)	0.04	117	30.8% (36)	0.04	236	29.2% (69)
36	117	33.3% (39)	0.04	114	35.1% (40)	0.04	231	34.2% (79)
48	118	39.8% (47)	0.05	114	36.0% (41)	0.04	232	37.9% (88)
Long-term Follow-up, Non-augmented								
24	96	34.4% (33)	0.05	98	31.6% (31)	0.05	194	33.0% (64)
36	87	39.1% (34)	0.05	87	40.2% (35)	0.05	174	39.7% (69)
48	76	47.4% (36)	0.06	81	40.7% (33)	0.05	157	43.9% (69)

Table 25 - Evolution of CDAI LDA or Remission Rates Through Week 48

DAS28-CRP ≤3.2 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
0	122	1.6% (2)	0.01	117	4.3% (5)	0.02	N/A	
4	115	16.5% (19)	0.03	113	8.0% (9)	0.03		
8	117	17.9% (21)	0.04	113	10.6% (12)	0.03		
12	119	26.1% (31)	0.04	119	15.4% (18)	0.03		
Long-term Follow-up, All completers								
24	118	30.5% (36)	0.05	117	31.6% (37)	0.05	235	31.1% (73)
36	114	33.3% (38)	0.04	107	37.4% (40)	0.05	221	35.3% (78)
48	117	42.7% (50)	0.05	111	37.8% (42)	0.05	228	40.3% (92)
Long-term Follow-up, Non-augmented								
24	95	36.8% (35)	0.05	98	32.6% (32)	0.05	193	34.7% (67)
36	85	36.5% (31)	0.05	82	42.7% (35)	0.05	167	39.5% (66)
48	75	49.3% (37)	0.06	79	40.5% (32)	0.06	154	44.8% (69)

Table 26 - Evolution of DAS28-CRP LDA or Remission Rates Through Week 48

The Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) is validated for hand-MRI. RAMRIS measures of inflammation and structural damage also correlate independently with physical function, pain and patient global assessments, with improvements in synovitis and bone erosion associated with improvements in patient reported outcomes. Early MRI erosion progression at 12 weeks is a sensitive predictor of structural damage at 1 year. MRI erosion progression (change > 0.5 in RAMRIS erosion score) by Week 12 is associated with higher disability at 2 years (HAQ), mirroring characteristics of those with 1-year x-ray progression (Ann Rheum Dis. 2017;76(6):992-997; Ann Rheum Dis. 2014;73(11):1968-1974).

In the ITT population, 216 patients had RAMRIS scores measured at baseline and Week 12 (treatment 109, control 107). Prespecified subgroup analyses included patients with an Erosive Phenotype (treatment 57, control 48), defined as synovitis score of 2 or more on any individual joint, at least 4 joints with a score of 1, or any joint with osteitis at baseline, as well as those that had failed only 1 prior b/tsDMARD (46 treatment, 36 control).

The proportion of bone erosion progressors by all patients and the subgroups of Erosive Phenotype and 1 prior b/tsDMARD are shown in **Table 27**.

Subgroup	n	Treatment % (n)	SE	n	Control % (n)	SE	p-value
All	108	16.7% (18)	0.04	105	20.0% (21)	0.04	0.2476
Erosive Phenotype	53	18.9% (10)	0.05	45	37.8% (17)	0.07	0.0156
1 b/tsDMARD	46	6.5% (3)	0.04	36	25% (9)	0.07	0.0099

Table 27 - Proportion of Bone Erosion Progressors (>0.05 Change in Erosion Score) from Baseline to Week 12 in All Patients and Subgroup of Erosive Phenotype

The mean score changes in bone erosion, synovitis and osteitis from baseline to Week 12 among all patients, patients and the subgroups is presented in **Table 28**.

Mean Change in Erosion Score at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.2	0.85	0.08	105	0.5	1.74	0.17	0.0618
Erosive Phenotype	53	0.3	1.09	0.15	45	1.1	2.51	0.37	0.0156
1 b/tsDMARD	46	0.0	0.60	0.09	36	0.8	2.57	0.43	0.0441
Mean Change in Synovitis Scores at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.0	1.64	0.16	105	0.1	1.51	0.15	0.2871
Erosive	53	-0.1	2.27	0.31	45	0.0	1.77	0.26	0.4345
1 b/tsDMARD	46	0.1	0.81	0.12	36	0.6	1.78	0.30	0.0900
Mean Change in Osteitis Scores at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.1	2.61	0.25	104	0.8	4.13	0.40	0.0662
Erosive	53	0.2	3.74	0.51	45	1.8	6.18	0.92	0.0450
1 b/tsDMARD	46	-0.3	2.22	0.31	36	1.1	4.92	0.82	0.0350

Table 28 - Mean Change in Erosion, Synovitis and Osteitis Scores at Week 12

Continuation of treatment with the SetPoint System was assessed at Week 24, 36 and 48 to evaluate Therapy Persistence. Therapy Persistence on stimulation therapy, and Therapy Persistence on Setpoint System alone (non-augmented) are summarized in **Table 29**.

Persistence	Week 24			Week 36			Week 48		
	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)
Yes: SetPoint as standalone therapy *(no augmentation)*	78.7% (96)	82.5% (99)	80.6% (195)	73.0% (89)	73.3% (88)	73.1% (177)	63.1% (77)	67.5% (81)	65.3% (158)
Yes: Augmentation *(SetPoint with b/tsDMARD additional csDMARD and/or steroid added after Week 12)*	19.7% (24)	15.8% (19)	17.8% (43)	25.4% (31)	23.3% (28)	24.4% (59)	35.2% (43)	29.2% (35)	32.2% (78)

Persistence	Week 24			Week 36			Week 48		
	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)
Augmentation with b/tsDMARD	13.9% (17)	10.0% (12)	12.0% (29)	20.5% (25)	18.3% (22)	19.4% (47)	26.2% (32)	23.3% (28)	24.8% (60)
Augmentation with additional csDMARD and/or steroid	7.4% (9)	6.7% (8)	7.0% (17)	5.7% (7)	7.5% (9)	6.6% (16)	13.1% (16)	10.0% (12)	11.6% (28)
Yes: SetPoint as standalone or augmentation therapy	98.4% (120)	98.3% (118)	98.3% (238)	98.4% (120)	96.7% (116)	97.5% (236)	98.4% (120)	96.7% (116)	97.5% (236)
No: VNS suspended, or device removed	1.6% (2)	1.7% (2)	1.7% (4)	1.6% (2)	3.3% (4)	2.5% (6)	1.6% (2)	3.3% (4)	2.5% (6)

Table 29 - Persistence with SetPoint Therapy (based on ITT)

Patient satisfaction was assessed at Week 24 using five-point Likert rating scale. Additionally, patients were asked a question about whether they would recommend the SetPoint System to family and friends (**Table 30**).

	TOL [1] (N=122)	COL [2] (N=120)	All (N=242)
How satisfied are you with the SetPoint System for treatment of RA?			
N [3]	119	114	233
Somewhat to very satisfied	90 (75.6%)	92 (80.7%)	182 (78.1%)
Neither satisfied nor dissatisfied	14 (11.8%)	12 (10.5%)	26 (11.2%)
Somewhat to very dissatisfied	15 (12.6%)	10 (8.8%)	25 (10.7%)
Would you recommend the SetPoint System to a family member or a friend?			
N [3]	118	114	232
Yes	108 (91.5%)	110 (96.5%)	218 (94.0%)
No	10 (8.5%)	4 (3.5%)	14 (6.0%)

Abbreviations: COL, Control to Open Label; TOL, Treatment to Open Label
[1] Treatment to Open Label (TOL): The TOL population comprises treatment patients from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises Control patients from ITT population who received non-active (sham) stimulation through Week12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL).

Table 30 - Patient Satisfaction and Recommendation at Week 24

Appendix H – Cybersecurity

IT Configuration

A guide for more advanced IT configuration of the SetPoint System can be found on the SetPoint Medical Website at https://spm.care/manuals. The IT guide contains the following information:

- Detailed technical descriptions of minimum networking requirements
- Diagrams for the home and healthcare use environment
- A list of all addresses and ports the SetPoint System uses for its connectivity
- Recommended networking encryption protocols
- Recommendations for IT-related cybersecurity hardening
- Details on data integrity and backup procedures
- Troubleshooting related to IT issues

Cybersecurity Software Updates

Known cybersecurity vulnerabilities found in the SetPoint System will be published as advisories on the SetPoint Medical website. Any advisories can be found at https://spm.care/cybersecurity-advisories. Software and firmware updates that remediate cybersecurity vulnerabilities can be obtained by bringing your SetPoint Medical devices to your healthcare professional.

Data Integrity, Backup, and Recovery

A fundamental tenet of the SetPoint System's data strategy is about what data is *not* collected or stored. Every effort is made to avoid collecting, transmitting, or storing data unless it is necessary to the functionality of the system. For example, none of the following pieces of information are ever stored on the Implant or Charger:

- Patient Names
- Usernames or Emails
- Location or Address Information
- Clinic Information
- Phone Numbers
- Date of Birth
- Race or Gender Information

Implant Integrity and Backups

The Implant ensures the integrity on all its non-volatile memory. In certain critical spaces, such as therapy parameters, redundant copies of data are kept. Where redundant data is available, and corruption or tampering is detected, an attempt will be made to restore a known-valid copy of the data. If corruption is detected on non-volatile program memory, the device will return to its bootloader – a state which is displayed on the Charger so that the user is made aware (see **Appendix A - Charger LED Status**).

Integrity checks are performed routinely, including every time an Implant is charged and every time an Implant powers up to perform autonomous stimulation. Therapy parameters are kept safe with redundant copies on the Implant. They are also preserved in the Cloud. Should all therapy parameters on the Implant be corrupted or erased, they will be automatically restored by Programmer fetching the data from the Cloud during the next clinic visit.

Charger Integrity and Backups

The Charger also ensures the integrity of all its non-volatile memory. In certain critical spaces, redundant copies of data are kept. Where redundant data is available, and corruption or tampering is detected, an attempt will be made to restore a known-valid copy of the data. If corruption is detected on non-volatile program memory, the device will return to its bootloader – a state which is displayed on the Charger so that the user is made aware (see **Appendix A - Charger LED Status**). Integrity checks are performed routinely, including every time the Charger is placed on the Docking Station.

Decommissioning and Sanitizing the Charger's Data

The Charger stores the following Implant information in its non-volatile memory:

- A cached Implant Event Log, including the last-connected Implant's Model ID and Serial Number
- Key information for encryption with the Implant

This data is erased when connected to a new Implant. Only authorized and authenticated healthcare professionals are allowed to issue commands to read this data. The Charger leverages chip Readout Protection (RDP) modes to prevent any debuggers from accessing this data. Attempts to access this data with a debugger will result in erasing all memory on the device. No explicit steps are needed to sanitize or decommission a Charger.

Decommissioning and Sanitizing the Implant's Data

The Implant does not support deleting its data. **Contact SetPoint Medical** to request a return merchandise authorization (RMA) for the explanted Implant, if removed.

Responding to Cybersecurity Events

If you suspect a cybersecurity event has occurred, **contact SetPoint Medical**. SetPoint Medical has a team that monitors for cybersecurity events and will promptly respond to any cybersecurity threats. If you believe you have discovered a cybersecurity vulnerability in a SetPoint Medical product, please follow SetPoint Medical's Coordinated Vulnerability Disclosure process which can be found at https://spm.care/security.

Software Bill of Materials

An up-to-date Software Bill of Materials (SBOM) can be found on the SetPoint Medical Website at https://spm.care/sbom.

Cybersecurity End-of-Support

Cybersecurity support is offered through the expected operating duration of the devices (i.e., 5 years for the Charger and 10 years for the Implant). During this time, patients and healthcare professionals can expect cybersecurity updates to the Implant and Charger to address any vulnerabilities that may be discovered.

SETPOINT SYSTEM

SURGEON

INSTRUCTIONS FOR USE

Read all instructions, warnings and cautions carefully.

Failure to do so may damage the SetPoint System,
cause it to malfunction or perform poorly, and could result in injury.

If you have any questions about the information contained in the **SetPoint System Surgeon Instructions for Use** (Surgeon IFU), please **contact SetPoint Medical**.

All SetPoint System Instructions for Use (IFUs) are available on the SetPoint Medical website.

If you experience any incident or problem related to the SetPoint System
that may pose a safety risk, report it to SetPoint Medical immediately.

Contact

SetPoint Medical Corporation
25101 Rye Canyon Loop
Valencia, CA 91355-5004
United States

setpointmedical.com
+1 661.339.7900
customersuccess@setpointmedical.com

Caution: Federal law restricts this device to sale by or on the order of a physician.

SURGEON QUICK REFERENCE GUIDE

SETPOINT SYSTEM PROCEDURE

CONFIRM CHARGER FIT

- Place the Charger around the patient's neck while they are seated upright.
- Verify that the magnetic latch closes and remains latched without discomfort.

See section **Charger Fit Confirmation** for more details.

SURGICAL PROCEDURE

See section **Implantation** for more details.

1. Nerve Exposure

- 1.2 in (3 cm) branch-free segment of left vagus nerve.

2. Implant Placement

- Place the Pod on the left vagus nerve.
- Insert the Implant into the Pod, with the head-shaped marking oriented rostrally.
- Visualize that nerve is seated through ends of Pod groove and is in Implant saddle.
- Ensure that no extra nerve branches or other structures are entrapped in Pod.

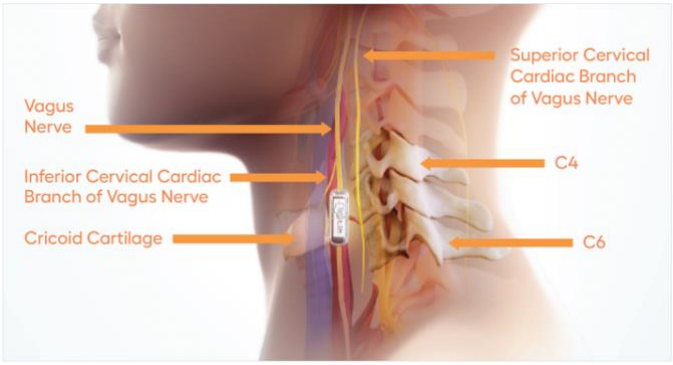
3. Closure

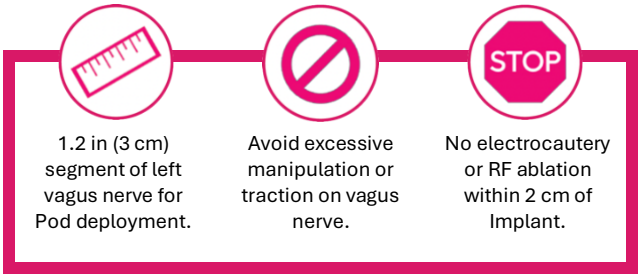
- Suture Pod through suture holes with non-absorbable 5-0 Prolene on a non-cutting needle and no more than 4 throws.
- Gently confirm Pod rotates and slides freely on the nerve.

IMPLANTATION LOCATION

- On the left cervical vagus nerve.
- Below both the inferior and the superior cervical cardiac branches.
- Ideally between the level of the C4 and C6 cervical vertebrae.

See section **Implantation Location** for more details.





It is important to read and understand the entire contents of the Surgeon IFU prior to use of the SetPoint System. Make sure to brief the patient on contraindications and warnings using section **Important Safety Information**.

SETPOINT® SYSTEM

Table of Contents

Introduction

This **SetPoint System Surgeon Instructions for Use** (Surgeon IFU) describes the operation and intended use of the SetPoint System and the surgical procedure for implantation. The SetPoint System is to be used only by physicians who have reviewed and understand this Surgeon IFU.

The table below shows the SetPoint System model numbers for the parts of the system that are described in this IFU.

Device Name	Model Number
Implant	M01
Charger	E04
Docking Station	C01

Table 1 - Device Names and Model Numbers

To reorder the Implant, **contact SetPoint Medical** and request Manufacturer Part Number SPM001.

Indication for Use

The SetPoint System is indicated for use in the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response, loss of response or intolerance to one or more biological or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs).

Pediatric Use

The SetPoint System is not intended for use in the pediatric population.

SetPoint System Description

The SetPoint System includes:

- The Implant (A) which is placed within a Pod (B) and implanted on the left vagus nerve in the neck (C)
- A Charger (D) with Docking Station (F)
- A Programmer (E)

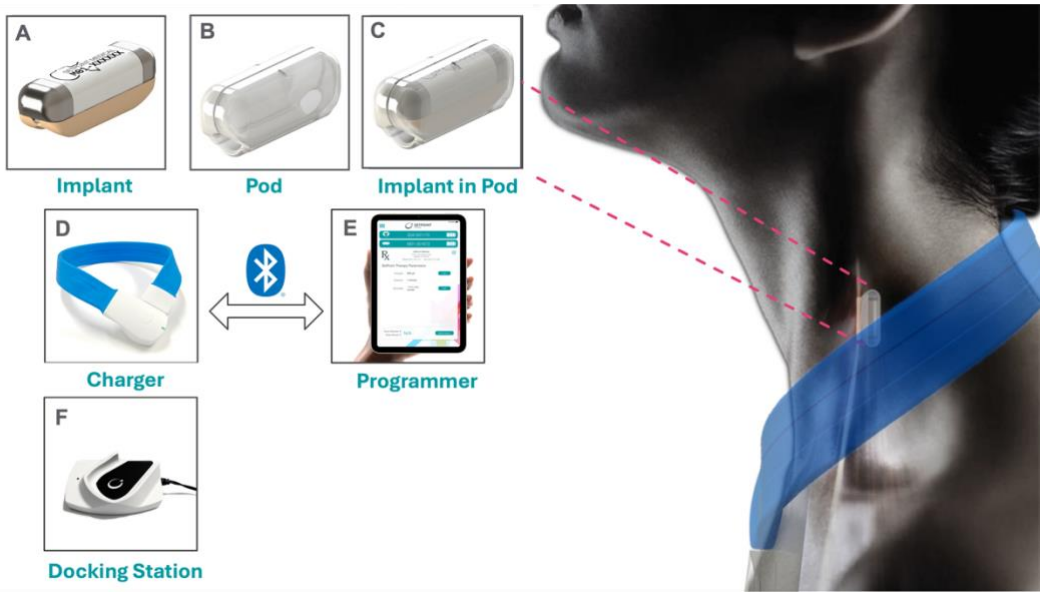


Figure 1 - SetPoint System and Components

Implant and Pod

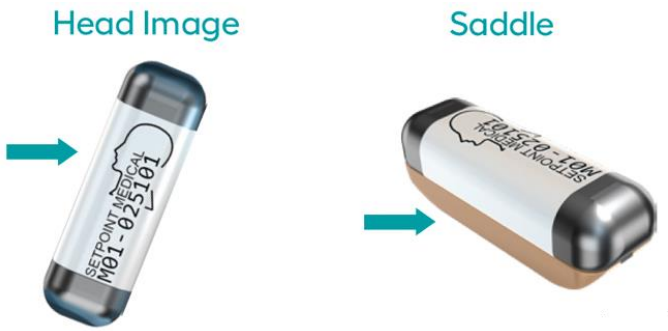


Figure 2 - Implant

The Implant is an integrated neurostimulation device. It is used to electrically stimulate the vagus nerve for 1 minute, every day. It is about 1 in (2.5 cm) long and weighs about 0.1 oz (3 g). The device is surgically implanted next to the vagus nerve on the left side of the neck. The Implant is placed inside a Pod, which is a flexible cover made of silicone. The Pod helps hold the Implant in place.

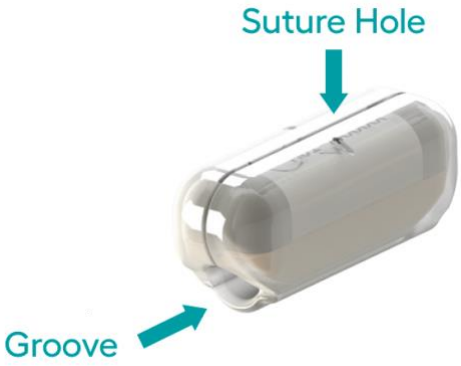


Figure 3 - Pod

The SetPoint System implantable components are supplied sterile, using an ethylene oxide (EO) process, and are only intended for single use. The Implant and two Pods (provided on plastic holders) are packaged in a sealed inner tray covered with an inner lid that prevents them from moving during transit (see **Figure 4**). The second Pod is provided for use only as a backup if the first Pod is damaged during deployment or while being sutured closed and is identical to the first Pod. The plastic holder is only intended for use during storage and must be discarded before the Pod is implanted. It is not meant for introduction into the surgical field.

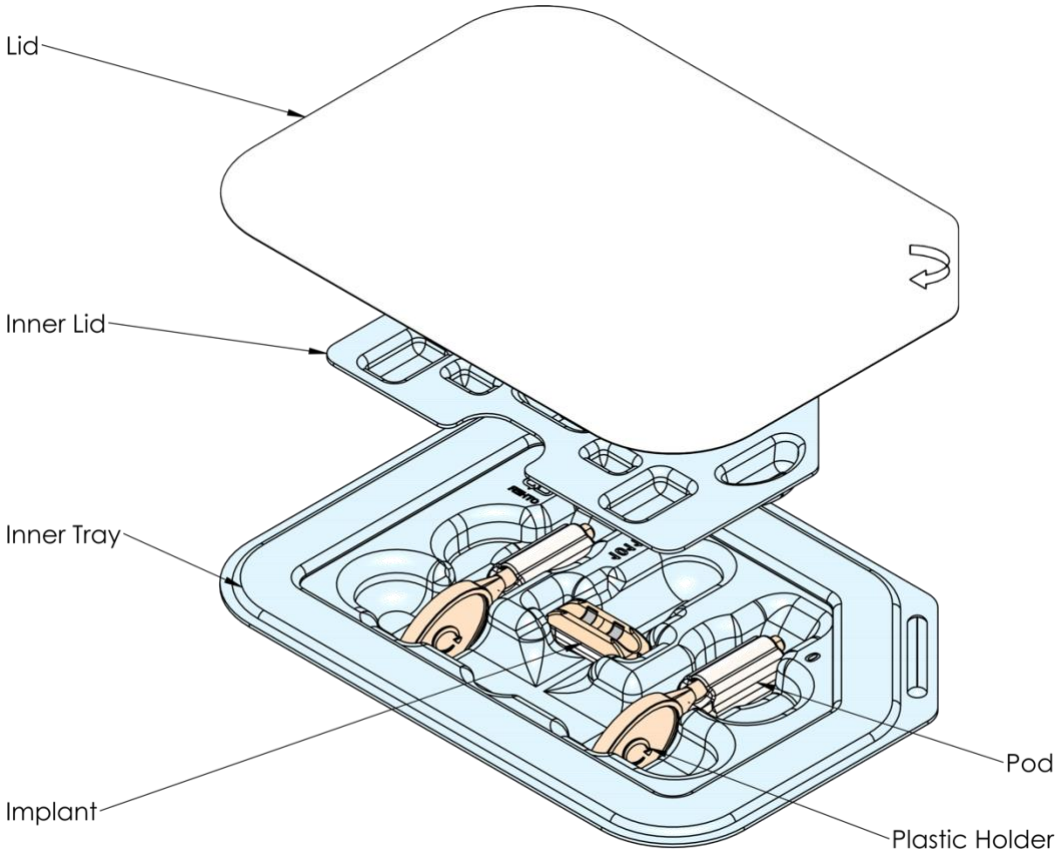


Figure 4 - Inner Tray Contents

The inner tray is packaged in a sealed outer tray, which displays the product labeling. The outer tray rests in a paperboard tray support and is packaged with a Patient ID Card inside a paperboard product box, which

also displays the product labeling. This product box is sealed with tamper evident labels. The product box must be stored within the following environmental conditions.

Temperature	Humidity	Altitude
50 to 104 °F (10 to 40 °C)	15 to 93 %RH	Up to 9,843 ft (3,000 m)

Table 2 – Storage Conditions

Charger and Docking Station

The Charger is a device worn around the patient's neck. It is used for charging the Implant at home and for programming the Implant at the clinic. The Docking Station is provided to charge and hold the Charger between uses.

For more information regarding the use of the Charger or Docking Station, please refer to the **SetPoint System Prescriber Instructions for Use** or **SetPoint System Patient Instructions for Use** which are available on the SetPoint Medical website.

Programmer

The Programmer is an app installed on an Apple iPad® that is only used by a trained healthcare professional. It is used with the Charger to program the Implant or to turn off or resume stimulation, if necessary. Additionally, it gives the healthcare professional information about the use of the Implant and Charger, such as how many doses have been delivered or missed, and Implant battery charge levels.

For more information regarding the use of the Programmer, please refer to the **SetPoint System Prescriber Instructions for Use** which is available on the SetPoint Medical website.

Patient Identification (ID) Card

The Patient ID Card is included in the Implant packaging. The Patient ID Card should be filled out per instructions that accompany the card (see **Figure 5**) and provided to the patient after the surgery, and before they leave the hospital. Device information, such as model number, serial number and device identifier, can be completed using one of four device stickers provided on the outer tray label in the Implant packaging (see **Figure 6**). Patients should be instructed to always have their Patient ID Card on hand and present it during security screenings, such as at airports. Additionally, the QR code on the card provides access to critical information regarding the Implant, which is necessary to ensure that any treatments are compatible with it. Instruct the patient to always present the Patient ID Card to healthcare professionals, dentists, or estheticians before pursuing any additional medical, medical imaging or beauty treatments. Neglecting to inform these professionals about the Implant may cause harm to the SetPoint System and/or may lead to complications with the treatment. If the patient changes their doctor or rheumatologist managing the SetPoint System, or loses their card, they should **contact SetPoint Medical for a replacement card**.

Figure 5 - Sample Patient ID Card (Front and Back)

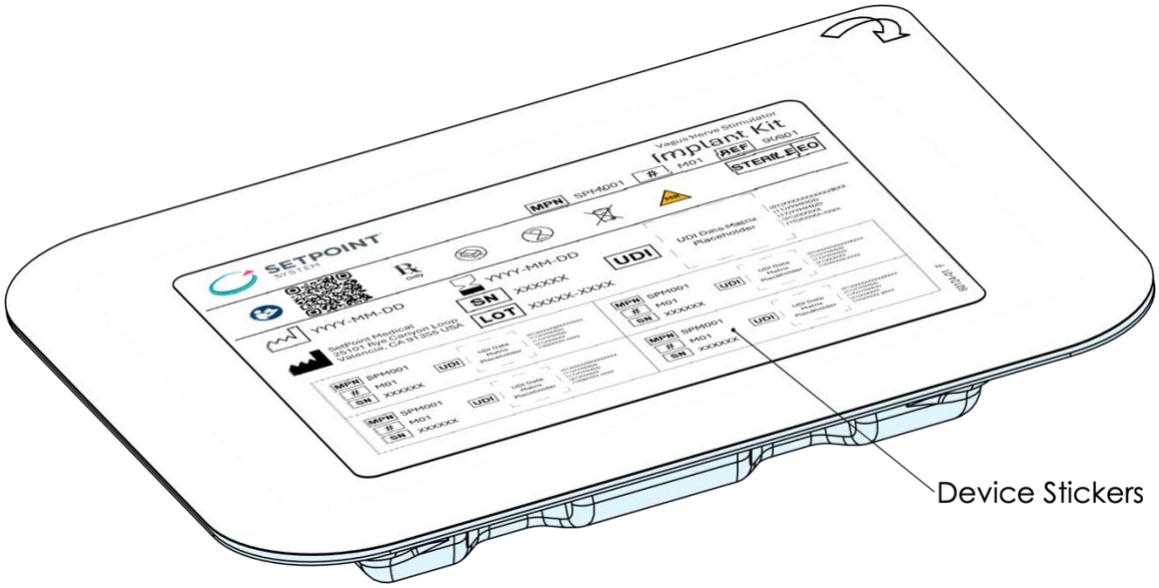


Figure 6 - Device Stickers on Outer Tray Label

Important Safety Information

Read all instructions, warnings and cautions carefully. If you have any questions, **contact SetPoint Medical**. If you do not follow these guidelines, the SetPoint System could get damaged, not work correctly, and/or result in harm.

Contraindications

There are certain situations in which the SetPoint System should not be used because the risk(s) are greater than the potential benefit(s).

The SetPoint System should not be used:

- If the patient has had certain health procedures that would interfere with how the device works, for example,
  - If they have had a bilateral or left cervical vagotomy.
  - If they have had their spleen removed (splenectomy).
- If you determine that it might not be safe for them to have the surgery, for example,
  - If they have spine disease in their neck that makes it risky to place a breathing tube (intubate).
  - If they cannot be safely given anesthesia for surgery.
- If they cannot safely use the SetPoint Charger, for example,
  - If their neck is too large to wear the SetPoint Charger.
  - If they have a pacemaker or a defibrillator implanted.

Warnings & Precautions

It is important that both you and the patient use the SetPoint System safely to avoid injury or damage to the SetPoint System or other devices. Here are some key safety tips:

- Instruct the patient to always present the Patient ID Card, prior to undergoing any treatment or diagnostic procedure, to healthcare professionals and providers such as physicians, dentists, imaging technicians (e.g., MRI, X-ray, computerized tomography), physical or occupational therapists, estheticians and beauty-care specialists. Failure to present the Patient ID Card may result in a treatment or procedure-related complication and/or may damage the SetPoint System (see **Medical Imaging Warnings** below).
- Instruct the patient not to scuba dive or enter a hyperbaric chamber after receiving the Implant. The safety of high pressure has not been established, and these conditions could damage the device.
- Do not use the Implant or Pod if either device shows damage, the packaging shows signs of significant damage, the sterile packaging is breached, the tamper evident label indicates that the package has been opened, or if the product is beyond its expiration date. If you do, you might implant a non-functional device or one with compromised sterility.
- Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do verify adequate vagus nerve exposure of at least 1.2 in (3 cm) prior to Pod placement. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do verify that the Implant and Pod are placed freely on the vagus nerve with no entrapped branches. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do not re-use the Implant or Pod with another patient. If you do, it will not be sterile.
- Adhere to local e-waste regulations when disposing of any part of the SetPoint System. If you do not, environmental contamination with hazardous substances can result.

Medical Imaging Warnings

There are various types of medical imaging technologies in common use. Although X-rays, computed tomography (CT), ultrasound imaging (sonography), positron emission tomography (PET) are all safe to perform after the patient receives their Implant, it is vital that they always show their Patient ID Card to any healthcare professionals performing these procedures. Specifically for magnetic resonance imaging (MRI), the patient must wait a minimum of two weeks after implantation before they are permitted to have an MRI scan. However, all MRI scans performed more than 14 days after implantation must meet the conditions outlined in the **SetPoint System Magnetic Resonance Imaging (MRI) Safety Information Manual**. This includes the fact that MRI scans must not overlap the time of stimulation of the Implant, which can be avoided by not performing the scan within ±1 hour from the time documented on the patient's Therapy Parameters Card. Note that if the Implant is suspended or expired, it will not deliver stimulation and this restriction is unnecessary. **In any case, as long as the patient is implanted, they must inform MRI personnel that the Implant is *MR Conditional*.**

Figure 7 - MR Conditional

⚠ **Warning: The SetPoint Charger and SetPoint Docking Station should never be brought near MRI machines because they are not safe for use in that environment. Thus, the Charger and Docking Station are referred to as MR Unsafe.**

Figure 8 - MR Unsafe

Medical Procedure Warnings

Instruct the patient to use caution with any medical procedure that introduces electrical current, electromagnetic radiation, or thermal energy into tissues in the neck area. The Implant may absorb, intensify, or reflect these energy sources, resulting in localized heating that could damage the device or nearby nerves and vascular structures. This damage may result in pain or discomfort, loss of vocal cord function, or possibly even life-threatening injury if there is damage to a blood vessel. Note that these risks are present whether the Implant is active or suspended. It is extremely important that they always show their Patient ID Card to any healthcare professional performing these procedures so that they can carefully evaluate potential risks due to interactions between the procedure and the SetPoint System. Before proceeding with any procedure that delivers energy to the tissues surrounding the Implant, the healthcare professional should consider alternatives that avoid energy transfer. Specific examples of higher risk procedures around the implantation site that need to be avoided because they could damage the Implant, cause it to malfunction, and/or result in harm including severe injury include:

⚠ **Warning:** Shortwave diathermy, microwave diathermy, ultrasound diathermy or other procedures that induce heat in internal tissues. This does not include diagnostic ultrasound which is permitted.

⚠ **Warning:** Electrosurgery/electrocautery, and ablative surgical techniques that utilize any form of electromagnetic radiation or electrical current to cut, coagulate, or thermally destroy tissues. **For**

electrocautery, do not use within 2 cm of the Implant[1]; if electrocautery is used within 2 cm of the Implant, the Implant will need to be replaced. If using monopolar electrocautery, place the return pad such that the current path is not across the Implant.

⚠ **Warning:** Transcutaneous electrical nerve stimulation (TENS), electroconvulsive therapy or other procedures that apply electrical current through skin surface electrodes.

⚠ **Warning:** Extracorporeal shock wave lithotripsy or other procedures that use pressure waves or induce mechanical forces to break up internal structures.

⚠ **Warning:** Radiation therapy, including forms of photon beam radiation therapy such as x-rays, gamma rays, proton beam therapy, brachytherapy, stereotactic radiosurgery, cobalt machines, and linear accelerators.

If the patient has had any of the above medical procedures around the implantation site, it is very important that, very soon thereafter, they discuss the procedure with their doctor or rheumatologist managing the SetPoint System in order for them to determine whether verification of Implant functionality is necessary.

Radio Frequency (RF) Warnings

The SetPoint System uses radio-frequency (RF) fields for communication between different parts of the system or when charging the Implant or Charger. These RF fields could disrupt the functioning of similar frequency-utilizing devices.

⚠ **Warning:** Instruct the patient not to use the Charger for charging the Implant near devices sensitive to RF interference, while travelling in vehicles such as cars, trains, boats, airplanes, or during any medical treatments, or in proximity to other medical devices.

⚠ **Warning:** The SetPoint System has not been tested with, and may affect the operation of, other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include, but are not limited to, sensing problems and inappropriate device responses.

⚠ **Warning:** The RF signals from the Charger could theoretically interfere with or be concentrated by other implanted devices such as neural stimulators or insulin pumps.

The Charger and Docking Station are vulnerable to electromagnetic interference from devices that emit RF fields, like cellphones and security scanners. Portable RF communications equipment (including peripherals such as antenna cables and external antennas), RFID scanners and card readers (including animal identification tag scanners) should be used no closer than 12 inches (30 cm) to any part of the Charger and Docking Station. Otherwise, degradation of the performance of this equipment could result.

⚠ **Warning:** If it is suspected that the Charger or Docking Station are not functioning correctly due to electromagnetic interference, try changing the patient's location, waiting until a later time, or turning off the suspected source of interference if possible. Use of the Charger or Docking Station adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such

---

[1] Safety testing was performed using 3 applications of 25 W bipolar and 30 W monopolar electrocautery each at 1 cm from the Implant. Exceeding this number of applications or power setting near the Implant may increase the risk of nerve injury or device failure.

use is necessary, the Charger and Docking Station should be observed to verify they are operating normally.

⚠ **Warning:** The Charger and Docking Station are intended for use indoors, for example in the home or clinic. They should not be used in environments where the intensity of electromagnetic disturbances is known to be high, such as near high-frequency surgical equipment or radio transmitters. They should also not be used in any environment with a posted FCC Notice, Caution or Warning sign indicating the presence of high-intensity radio frequency (RF) fields that surpass normal public exposure limits. These areas are typically indicated by restricted environment signs like those in **Figure 9**. After receiving the Implant, the patient should not enter these areas without seeking medical guidance first. Exposure to high levels of RF could cause the Implant to malfunction or lead to tissue damage in the vicinity of the device.

Figure 9 - Restricted Environment Signage

Education, Training, and Services

In addition to the information provided in this Surgeon IFU, supplementary training materials including, but not limited to, a training presentation, surgical videos, and a training model are available and can be provided upon request. Additional training, if requested, can be arranged with your local SetPoint Medical representative.

Surgical Procedures

Surgical procedures for the SetPoint System should be performed by a surgeon with expertise in the surgical anatomy of the carotid sheath, its contents, and its surrounding structures, and with experience in safe dissection and manipulation of these structures and of cranial nerves such as the vagus nerve.

Implantation Location

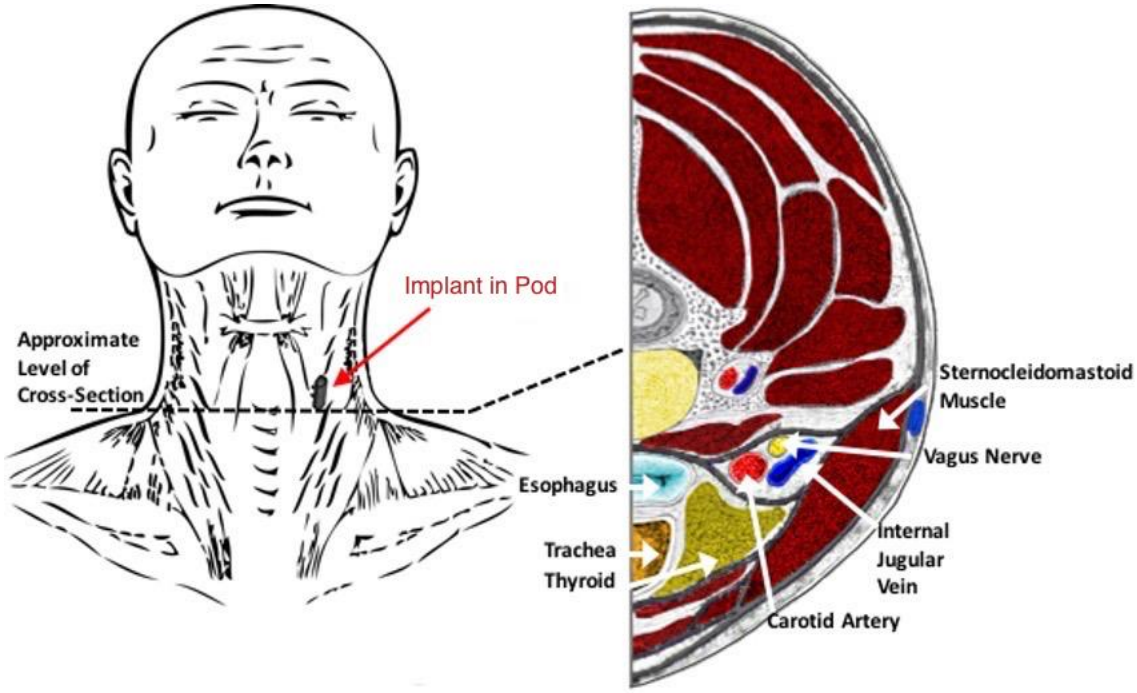


Figure 10 - Implant Location

The Implant must be placed on a segment of the left cervical vagus nerve that is at least 1.2 in (3 cm) long and free from any branches. A suitable segment is typically half-way up between the clavicle and the mastoid process and below both the inferior and superior cervical cardiac branches.

Ideal placement for the Implant to optimize communication with the Charger is between the level of the C4 and C6 cervical vertebrae. The Implant should never be placed below the level of the C7 cervical vertebra. An example placement is illustrated in **Figure 11**.

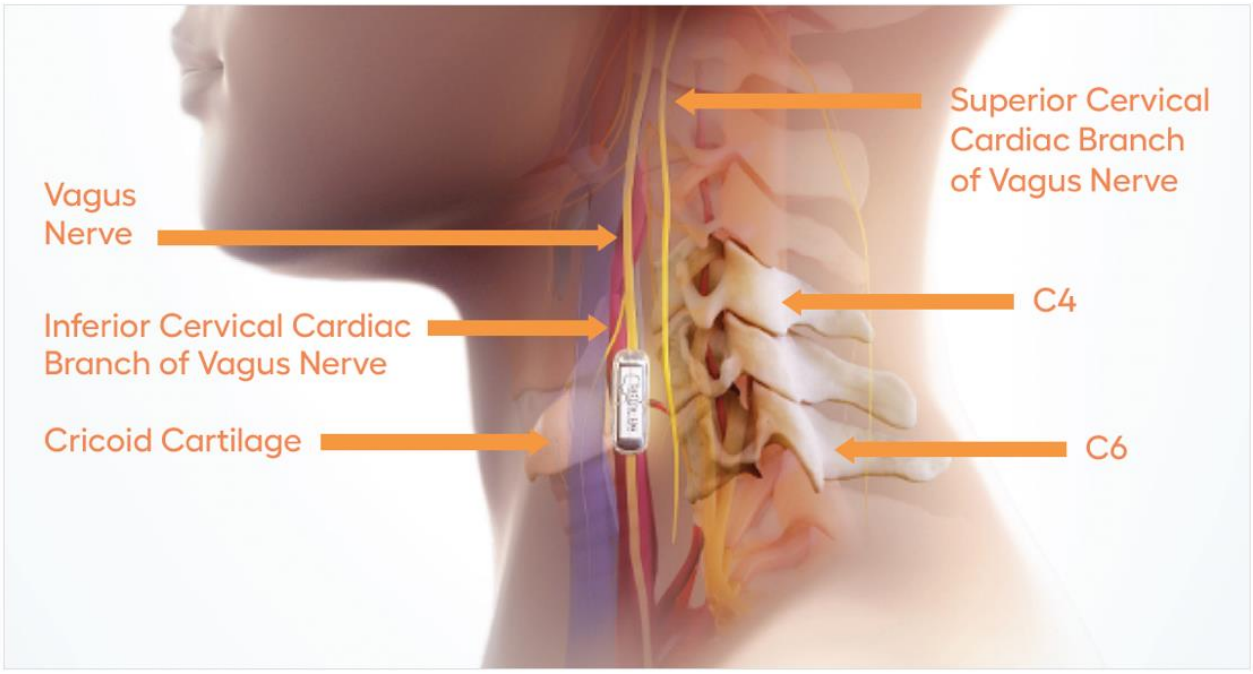


Figure 11 - Relationship Between Implant Implantation Location and Vagus Nerve Branches

Charger Fit Confirmation

To confirm fit of the Charger prior to the implantation procedure, it is recommended that the following steps be performed:

1. Prior to the implant procedure, either place the Charger, or instruct the patient to place the Charger around their neck while they are seated upright.
2. Verify that the magnetic latch closes and remains latched without discomfort.
3. Remove the Charger or instruct the patient to remove the Charger.

Implant Preparation

⚠ **Warning:** Do not use the Implant or Pod if either device shows damage, the packaging shows signs of significant damage, the sterile packaging is breached, the tamper evident label indicates that the package has been opened, or if the product is beyond its expiration date. If you do, you might implant a non-functional device or one with compromised sterility.

1. Carefully open the product box and remove the outer tray. Set aside the Patient ID Card to fill out after the surgery is complete.
2. The outer tray should be opened by pulling the tab on the lid as shown in **Figure 12**. Set aside the outer tray lid and label with the device stickers on it (see **Figure 6** on page 9), to adhere to the Patient ID Card.

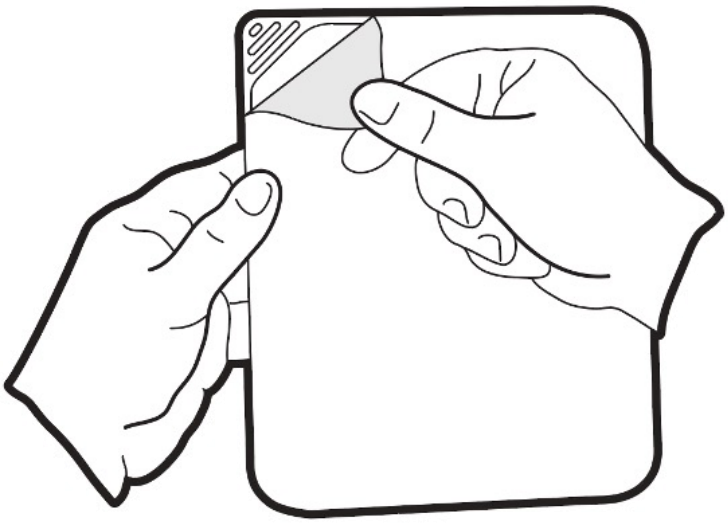


Figure 12 - Opening Tray by Pulling Tab

3. Present the outer tray so that the inner tray can be removed in the sterile field.
4. The inner tray should be opened by pulling the tab on the lid as shown in **Figure 12**.
5. Remove the inner lid and discard (see **Figure 4** on page 7).
6. Place the inner tray on the surgical tray or other sterile surface in the sterile field.
7. If at any point during the surgical procedure the Implant is dropped from a height of over 6 in (15 cm), discard the Implant and utilize the backup.

Implantation

⚠ **Warning:** Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.

Using standard surgical techniques, make a single transverse incision on the left ventral surface of the neck, dissect the fascia and musculature to expose the carotid sheath, and identify the vagus nerve. Then:

1. Locate and expose a segment of the left vagus nerve that is free of branches by circumferentially dissecting the surrounding tissue.

⚠ **Warning:** Do verify adequate vagus nerve exposure of at least 1.2 in (3 cm) prior to Pod placement. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.

2. Confirm with a surgical ruler that at least 1.2 in (3 cm) of nerve segment has been exposed to allow for manipulation and insertion of the Pod.
3. If using vessel loops, place under the nerve utilizing standard surgical techniques.
4. Remove a Pod from its plastic holder and discard the plastic holder (see **Figure 4** on page 7).
5. The following are recommended techniques for Pod deployment to accommodate anatomical variations.
    a. Flat Method:
        i. Hold the Pod open facing upwards (see **Figure 13a**) and use forceps to clamp it in the open position along its midline (see **Figure 13b**).
        ii. Insert the Pod under the nerve (see **Figure 13c**) and align it such that the nerve is positioned at the Pod groove (see **Figure 3** on page 7 and **Figure 13d**).

iii. Slowly release the forceps, allowing the Pod to return to its original shape (see **Figure 13e**), closing around the nerve (see **Figure 13f**). If needed, use forceps to gently maneuver the Pod so that nerve is resting in the Pod groove and the Pod opening is facing upwards.

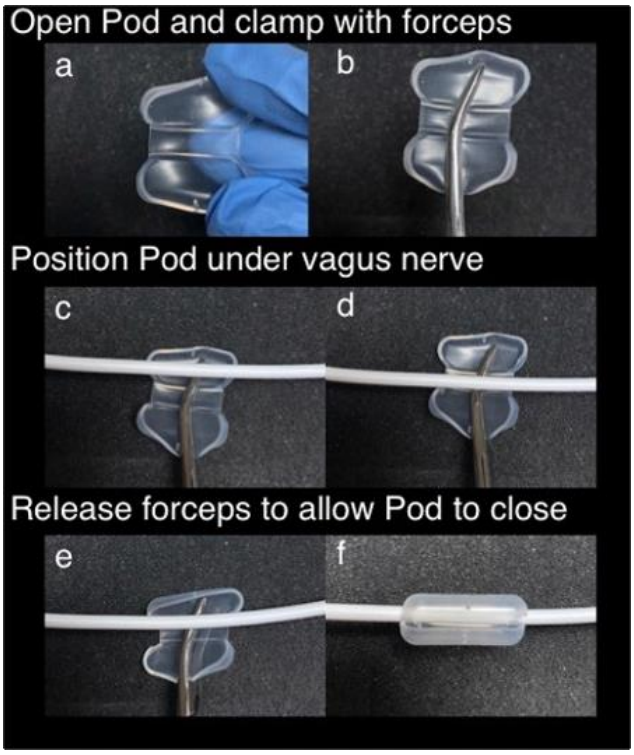


Figure 13 - Pod Implantation: Flat Method

b. Fold Method:
   i. Hold the Pod open facing downwards by pressing on both sides (see **Figure 14a**).
   ii. Fold the Pod off axis (see **Figure 14b**) and use curved forceps to clamp the Pod perpendicular to the Pod groove (see **Figure 3** on page 7 and **Figure 14c**). Turn the forceps so that the Pod opening is facing upwards (see **Figure 14d**).
   iii. Introduce the Pod under the vagus nerve, gently rotating the forceps by approximately 90 degrees to minimize touching the nerve.
   iv. Once the mid-line is positioned under the nerve, rotate the Pod so that the opening is facing upwards (see **Figure 14e**).
   v. Slowly release the forceps, allowing the Pod to return to its original shape (see **Figure 14f** and **Figure 14g**), closing around the nerve (see **Figure 14h**). If needed, use forceps to gently maneuver the Pod so that nerve is resting in the Pod groove and the Pod opening is facing upwards.

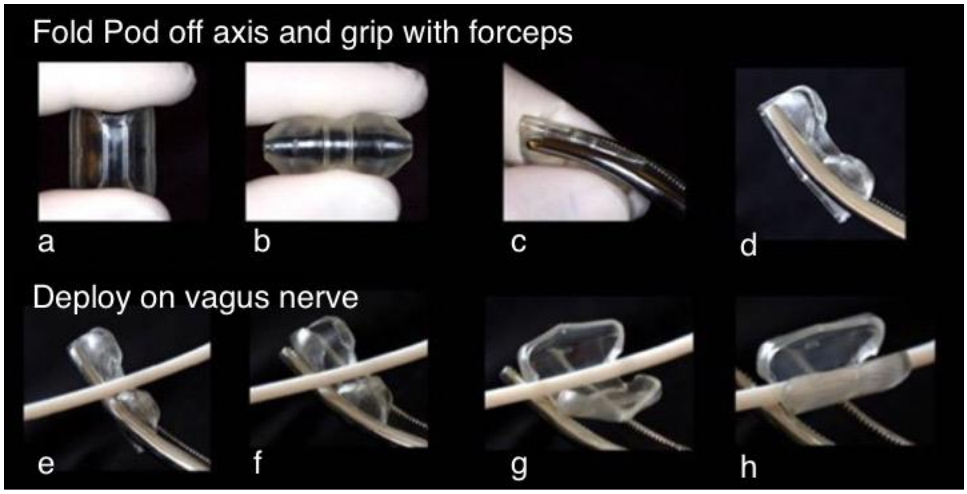


Figure 14 - Pod implantation: Fold Method

6. Insert the Implant into the Pod, (see **Figure 16a-d**) with the head-shaped marking on the Implant oriented rostrally (see **Figure 15**).

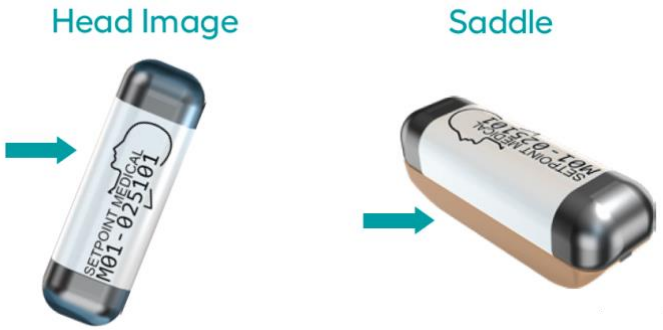


Figure 15 - Head-shaped Marking Indicating Rostral End of the Implant

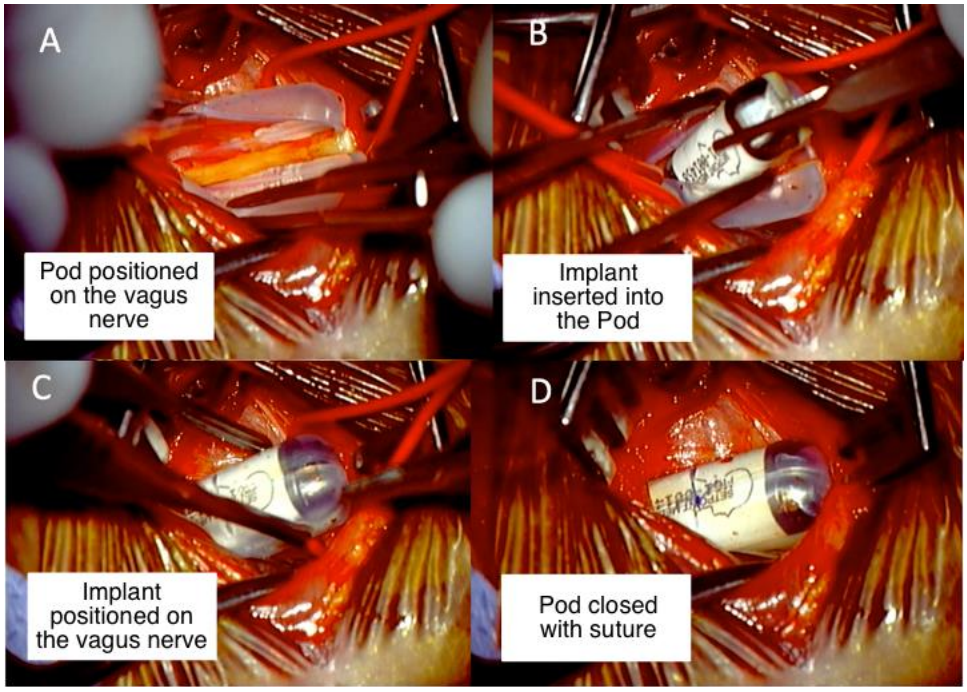


Figure 16 - Pod and Implant Implantation Method

7. Close the Pod around the Implant.
8. While minimizing Pod movement, suture the Pod closed through the suture hole in the Pod (see **Figure 17**) with a non-absorbable 5-0 Prolene suture on a non-cutting needle. Limit the number of throws in the knot to a maximum of four to avoid excessively pulling on the device or nerve.

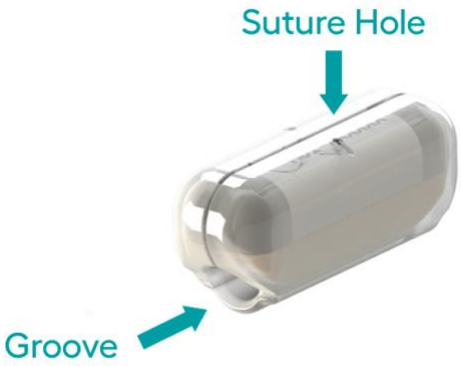


Figure 17 - Pod Suture Hole

⚠ **Warning:** Do verify that the Implant and Pod are placed freely on the vagus nerve with no entrapped branches. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.

9. Visualize that the nerve is seated through the ends of the groove of the closed Pod and is in the Implant saddle. Ensure that there are no extra nerve branches or other structures entrapped in the Pod.
10. Verify the closed Pod does not constrict the nerve or vascular tissue by using either a gentle sliding movement of the Pod on the nerve or a slight rotation of the Pod.

Using standard surgical techniques, close the musculature, fascia and skin. Frequent irrigation of the implantation site with generous amounts of bacitracin or equivalent solution can be performed prior to closure for infection control. To minimize scarring, the incision should be closed with cosmetic closure techniques.

Fill out the Patient ID Card and adhere one of the device stickers (see **Figure 18**) onto the correct location on the card (see **Figure 19**). The filled-out card should be provided to the patient after surgery.

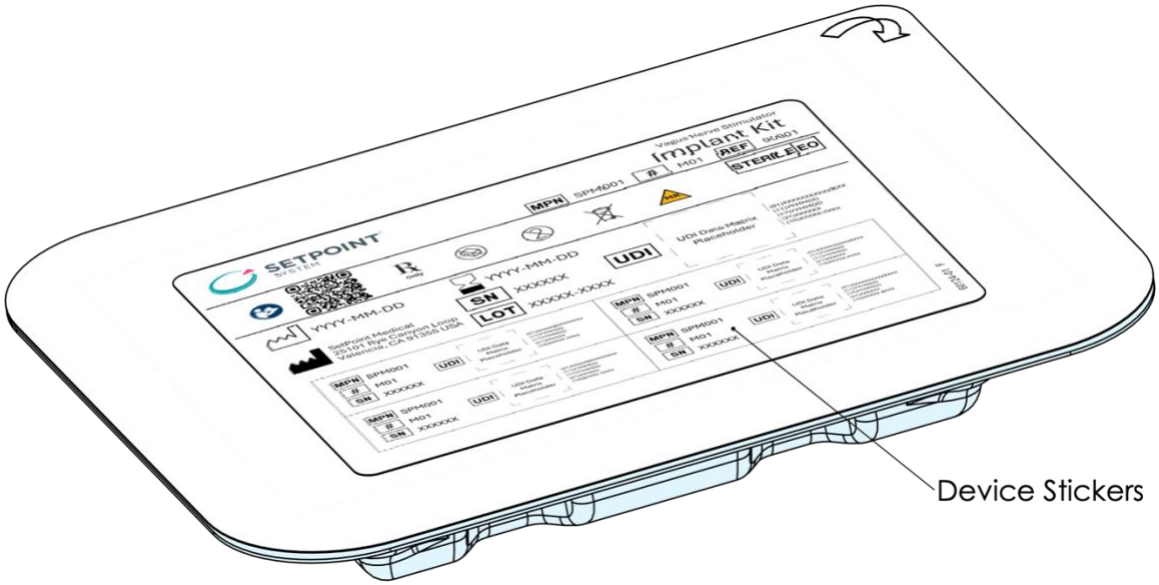


Figure 18 - Device Stickers on Outer Tray Label

Figure 19 - Sample Patient ID Card (Front and Back)

Explantation and Reimplantation

The adverse events associated with explantation or reimplantation are similar to those associated with implantation, but the risk of occurrence of such events is likely to be greater because the presence of scarring around the chronically implanted device makes removal more difficult. If Implant removal is contemplated, SetPoint Medical should be notified prior to explantation or reimplantation surgery.

Therapy programming on the Implant should be suspended, if possible, prior to surgery.

⚠ **Warning:** Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.

If performing a reimplantation, prepare the new Implant as per instructions in section **Implant Preparation**. Using standard surgical techniques, make a single transverse incision on the left ventral surface of the neck, dissect the fascia and musculature to expose the carotid sheath. Then:

1. Expose the Implant in the Pod by incising any tissue capsule surrounding it along the Pod opening (see **Figure 17** on page 19) with the suture visible.
2. Cut the suture and open the Pod.
3. Remove the Implant from the Pod.
4. If performing an explantation, cut the Pod in halves by cutting parallel to the groove in the Pod (see **Figure 17** on page 19) and then remove the halves.
5. If performing a reimplantation, inspect the Pod for damage, specifically the integrity of the suture holes.
    - If the Pod is undamaged, leave it in place, place the new Implant by following steps 6-10 in the **Implantation** section (page 16)
    - If the Pod is damaged, cut the Pod in halves by cutting parallel to the groove in the Pod (see **Figure 17** on page 19) and then remove the halves. Place the new Pod and Implant by following steps 3-10 in the **Implantation** section (page 16).

Using standard surgical techniques, close the musculature, fascia and skin. Frequent irrigation of the incision site with generous amounts of bacitracin or equivalent solution can be performed prior to closure for infection control. To minimize scarring, the incision should be closed with cosmetic closure techniques.

The old Patient ID Card should be retrieved and discarded. If performing a reimplantation, fill out the new Patient ID Card and adhere one of the device stickers (see **Figure 18**) from the new Implant onto the correct location on the card (see **Figure 19**). The new, filled-out card should be provided to the patient after surgery.

⚠ **Warning:** Do not re-use the Implant or Pod with another patient. If you do, it will not be sterile.

⚠ **Warning:** Adhere to local e-waste regulations when disposing of any part of the SetPoint System. If you do not, environmental contamination with hazardous substances can result.

Contact SetPoint Medical to request a return merchandise authorization (RMA) for the explanted Implant and Pod, if removed.

Guidelines for Patient Follow-up

Following the implant procedure, the patient should be cleared for programming of SetPoint System after confirming incision healing, and post-operative recovery. Subsequent follow-up schedule should be determined by the Surgeon based on patient recovery following the implant procedure.

Patient Counseling Information

Patients should be counseled to always carry and present the Patient ID Card to healthcare professionals and providers such as physicians, dentists, imaging technicians (e.g., MRI, X-ray, computerized tomography), physical or occupational therapists, estheticians and beauty-care specialists before pursuing any additional medical, medical imaging or beauty treatments. Failure to present the Patient ID Card may result in a treatment or procedure-related complication and/or may damage the SetPoint System (see sections **Patient Identification (ID) Card** and **Medical Imaging Warnings**). If the patient or

healthcare professional requires the stimulation to be suspended, the patient should **contact the Prescriber's office**.

In case of post-operative concerns or issues, the patient must be counseled to immediately notify the Surgeon for further follow-up.

Appendix A – Explanation of Symbols Used on Packaging and Devices

Symbol	Title	Reference	Description
21 CFR 801.109: Prescription Devices			
	Prescription Only	(b) (1)	Caution: Federal law restricts this device to sale by or on the order of a physician
ASTM F2503			
	Magnetic Resonance (MR) Conditional	Fig. 5	An item with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields and the radiofrequency fields
	Magnetic Resonance (MR) Unsafe	Fig. 9	An item which poses unacceptable risks to the patient, medical staff or other persons within the MR environment
WEEE Directive 2012/19/EU			
	Symbol for the marking of EEE	Annex IX	Separate collection for electrical and electronic equipment
IEC 60417			
	Non-ionizing Electromagnetic Radiation	5140	To indicate elevated, potentially dangerous, levels of non-ionizing radiation
	For Indoor Use Only	5957	To identify electrical equipment designed primarily for indoor use
IEC 60529			
IP22	Degree of Protection	N/A	Protected against solid foreign objects of 0.5 in (12.5 mm) Ø and greater; Protection against vertically falling water drops when enclosure is tilted up to 15°.
ISO 15223-1: 5.1. Manufacture			
	Manufacturer	5.1.1	Indicates the medical device manufacturer
	Date of Manufacture	5.1.3	Indicates the date when the medical device was manufactured
	Use-By Date	5.1.4	Indicates the date after which the medical device is not to be used
	Batch Code	5.1.5	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Catalog Number	5.1.6	Indicates the manufacturer's catalog number so that the medical device can be identified
	Serial Number	5.1.7	Indicates the manufacturer's serial number so that a specific medical device can be identified

	Model Number	5.1.10	Indicates the model number or type number of a product
ISO 15223-1: 5.2. Sterility			
	Sterilized Using Ethylene Oxide	5.2.3	Indicates a medical device that has been sterilized using ethylene oxide
	Do Not Use If Package Is Damaged and Consult Instructions for Use	5.2.8	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information
ISO 15223-1: 5.3. Storage			
	Temperature Limit	5.3.7	Indicates the temperature limits to which the medical device can be safely exposed
	Humidity Limitation	5.3.8	Indicates the range of humidity to which the medical device can be safely exposed
	Atmospheric Pressure Limitation	5.3.9	Indicates the range of atmospheric pressure to which the medical device can be safely exposed
ISO 15223-1: 5.4. Safe Use			
	Do Not Re-Use	5.4.2	Indicates a medical device that is intended for one single use only
ISO 15223-1: 5.7. Others			
	Unique Device Identifier	5.7.10	Indicates a carrier that contains unique device identifier information
ISO 7010			
	Refer to Instruction manual/booklet	M002	To signify that the instruction manual/booklet must be read
	General Warning Sign	W001	To signify a general warning
N/A			
	Manufacturer Part Number	N/A	Indicates the manufacturer part number of a product

Applicable Standards and Regulations

21 CFR 801 Medical Devices – Labeling

ASTM F2503 – 23 Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

Directive 2012/19/EU of the European Parliament and of the Council of 4 July 2012 on waste electrical and electronic equipment (WEEE)

IEC 60417:2024 Graphical Symbols for use on Equipment

IEC 60529:1989/AMS2:2013/COR1:2019 Degrees of protection provided by enclosures (IP Code)

ISO 15223-1:2021 Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements

ISO 7010:2019 Graphical symbols – Safety colors and safety signs – Registered safety signs

Appendix B – Clinical Studies Summary

The SetPoint System has been evaluated in two U.S. clinical studies with a total of 256 implanted patients. The Pilot study (SPM-008) enrolled 14 multi-drug refractory RA patients to assess the safety and feasibility of implanting the SetPoint System, and the pivotal RESET-RA study (SPM-020) implanted 242 RA patients with inadequate response or intolerance to one (1) or more biological or targeted synthetic DMARDs to evaluate safety and efficacy of the SetPoint System.

At the time of FDA review for the SetPoint System, patients on average had been living with the Implant and receiving stimulation for longer than 1 year, with some patients, those enrolled in the Pilot study, receiving treatment for over 5 years.

This section will focus primarily on the RESET-RA study and will briefly review the Pilot study. Full analysis of the Pilot study is published in Genovese MC, Gaylis NB, Sikes D, et al. Lancet Rheumatology 2020;2(9):e527-e538.

Pilot Study (SPM-008)

Fourteen patients with multi-drug refractory RA underwent implantation with the SetPoint System in a first in human feasibility and safety study. The primary objective of the study was to determine the safety and tolerability of SetPoint System. Secondary endpoints included measurements of standard RA clinical outcomes as well as biomarker analysis of systemic inflammation.

The patients enrolled in the study were randomized to receive daily active stimulation of either 1 min QD (n=6) or 1 min QID (n=4), and non-active (sham) stimulation of 0 min QD (n=4). Efficacy outcomes presented include analysis from QD active and sham stimulation as QID dosing is not indicated for the SetPoint System. Due to the low number of patients in each group, statistically significant differences between groups were not expected, though trends that may indicate efficacy were noted.

There were no device-related adverse events noted during the conduct of the Pilot study. Treatment emergent adverse events showed no unusual adverse events during the study other than those related to the device implantation. The implantation procedure was generally well tolerated, and no perioperative infections were observed.

Six clinical adverse events associated with the implantation procedure were observed. All the observed adverse events were similar to observations documented in prior, published studies of other VNS systems or in other common surgical procedures, except for one occurrence of Horner's Syndrome, which resolved without permanent clinically significant sequelae prior to end of study. A separate incident of postoperative left vocal cord paresis occurred in this study, which is an adverse event that has been previously reported in association with vagus nerve surgery. All adverse events resolved over time and there were no permanent, clinically-significant sequalae documented.

There were no adverse, clinically significant changes noted for safety laboratory studies including CBC, electrolytes, renal function and urinalyses. There were no clinically significant changes noted for vital signs and physical examination. Cardiac safety monitoring included 12 lead ECG, rhythm strips collected during delivery of stimulation, and continuous, remote telemetry monitoring. Testing revealed no clinically significant, device associated alterations in the ECG.

Disease activity, as measured by signs and symptoms of Rheumatoid Arthritis, was evaluated using the DAS28-CRP (Disease Activity Score based on 28 joint count and C-reactive protein) as well as CDAI

(Clinical Disease Activity Index). At Week 12, 4 out of 6 patients in the QD group had changes in DAS28-CRP that exceeded the minimal clinically important difference (MCID) of -1.2 and the group mean average change in DAS28-CRP also exceeded -1.2. None of the 4 sham stimulated patients had changes in DAS28-CRP that exceeded the MCID of -1.2. Very similar results were observed when disease activity was scored using the CDAI metric, with the same number of actively stimulated QD patients exceeding the MCID of 12. None of the sham stimulated patients had changes in CDAI that exceeded the MID of -12.

An ex vivo bioassay using lipopolysaccharide (LPS)-elicited cytokine production by monocytes in culture showed that there was a substantial decrease in a subset of proinflammatory cytokines, including IL-1β, IL-6, IL-17, IL-23, and TNF-α, which are known to be relevant in RA pathophysiology at the Week 12 visit compared to Day 0 Visit. These cytokines were reduced in QD stimulated group but not in the sham stimulated group (**Figure 20**).

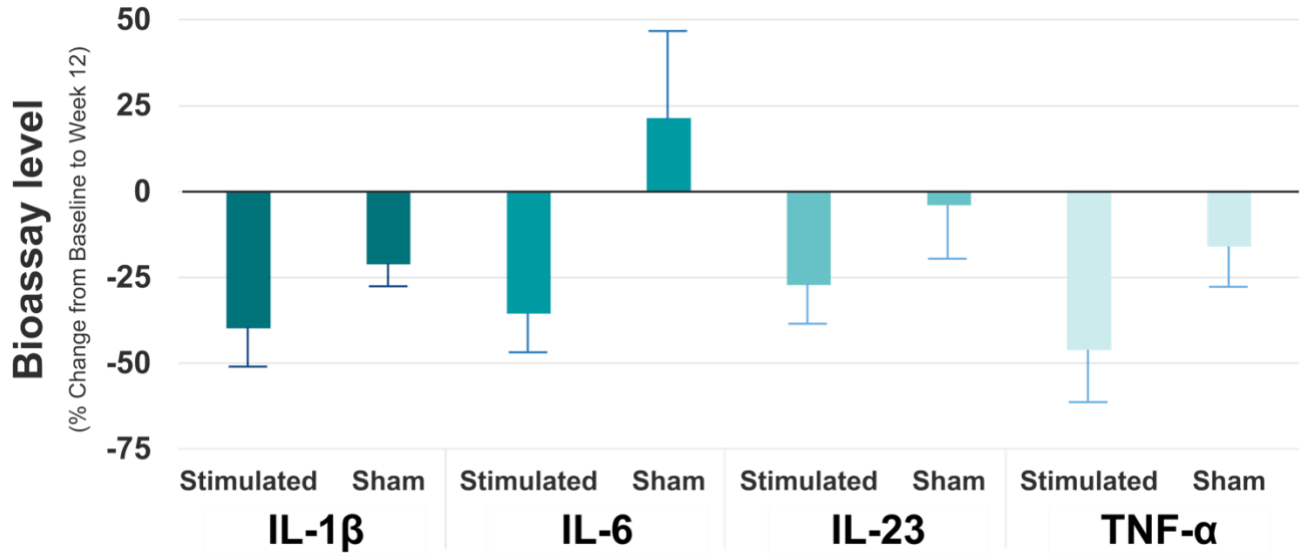


Figure 20 - Percent change from the Day 0 visit in proinflammatory cytokines levels in the TruCulture ex vivo bioassay (mean ± SME)

The primary endpoint of the Pilot study was to assess the overall safety and tolerability of the implantation surgical procedure, the device itself, and the active treatment, and, secondarily, the impact of active stimulation on RA clinical disease activity. Overall, the primary objective of the study was met as the use of the SetPoint System was well tolerated and showed initial clinical and biomarker efficacy in this group of multi-drug refractory RA patients.

RESET-RA Study (SPM-020)

RESET-RA study is a pivotal trial to assess the safety and efficacy of the SetPoint System for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response, loss of response or intolerance to at least one (1) biological or targeted synthetic DMARD (b/tsDMARD). The study enrolled 242 implanted patients across 41 study sites across the United States.

At the time of FDA review, data from the RESET-RA study was available for follow-up visits through Week 48.

Study Design

RESET-RA is a randomized, sham-controlled, double-blind, multicenter, pivotal study with 12-week follow-up for the primary efficacy endpoint, followed by one-way crossover of the control group and a 252-week open-label follow-up of all patients on active stimulation for long-term safety and effectiveness (**Figure 21**).

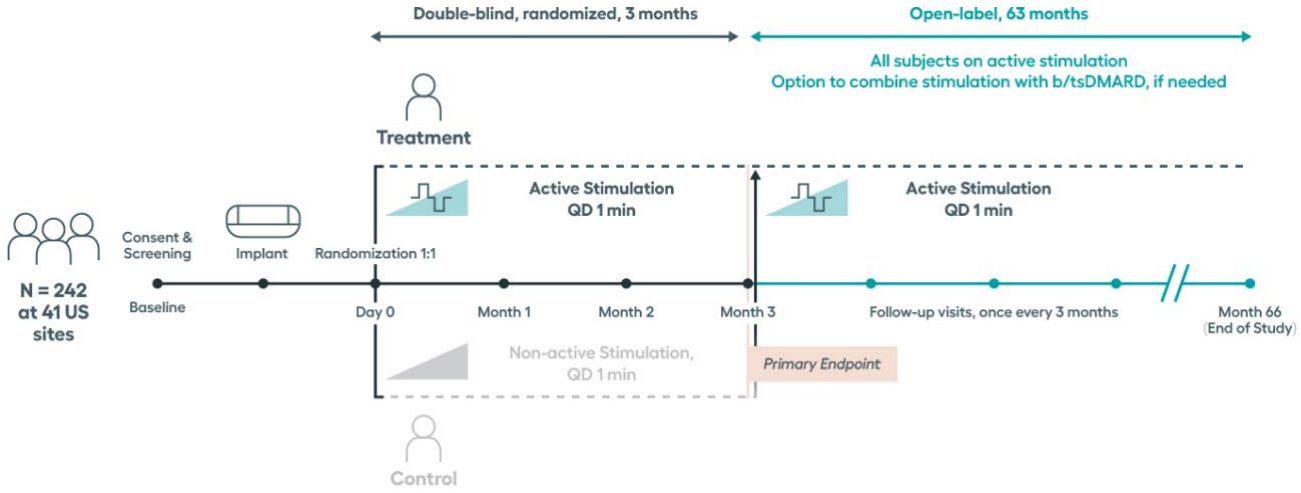


Figure 21 - RESET-RA Study Schematic

Enrollment in the RESET-RA study was limited to patients meeting eligibility criteria.

Key inclusion criteria for participation in RESET-RA included:

- 22-75 years of age at informed consent
- Moderate to severe RA, defined as at least 4/28 tender and 4/28 swollen joints
- Demonstrated inadequate response, loss of response, or intolerance to 1 or more b/tsDMARDs
- Receiving treatment with at least 1 conventional synthetic DMARD for at least 12 weeks and on a continuous non-changing dose and route of administration for at least 4 weeks prior to informed consent and able to continue the same stable dose through Week 12. Missing up to 2 doses due to COVID-19 vaccination was acceptable, except during the 4 weeks preceding informed consent.

Key exclusion criteria included:

- Current, regular use of nicotine-containing products, and lack of agreement to abstain from using nicotine-containing products throughout study participation
- Untreated or poorly controlled psychiatric illness or history of substance abuse
- Significant immunodeficiency due to underlying illness
- History of stroke or transient ischemic attack, or diagnosis of cerebrovascular fibromuscular dysplasia
- Clinically significant cardiovascular disease
- Neurological syndromes, including multiple sclerosis, Alzheimer's disease, or Parkinson's disease
- Uncontrolled fibromyalgia
- History of left or right carotid surgery
- History of unilateral or bilateral vagotomy, partial or complete splenectomy
- Recurrent vasovagal syncope episodes
- Hypersensitivity/allergy to MRI contrast agents and/or unable to perform MRI

All patients were required to remain on a stable background dose of at least 1 conventional synthetic DMARD through the primary endpoint evaluation. All patients were washed off their b/tsDMARDs prior to undergoing implantation procedure and considered enrolled once implantation is completed. Use of b/tsDMARDs from implantation procedure through Week 12 was not allowed. Addition of RA treatment, including adjunctive use of b/tsDMARD in combination with stimulation by SetPoint System, was allowed at any time after completion of Week 12 assessments if the patient experienced worsening of RA symptoms or did not experience adequate clinical improvement.

Demographics

Baseline demographics of patients in RESET-RA study, distributed by treatment and control group, are presented in **Table 3**.

	Treatment (N=122)	Control (N=120)	All (N=242)
Age (years)			
Mean (SD)	55.8 (10.3)	55.5 (10.5)	55.7 (10.4)
Median	57.0	56.5	57.0
Min, Max	25, 75	30, 75	25, 75
Gender			
Male	24 (19.7%)	10 (8.3%)	34 (14.0%)
Female	98 (80.3%)	110 (91.7%)	208 (86.0%)
Ethnicity			
Hispanic or Latino	23 (18.9%)	22 (18.3%)	45 (18.6%)
Not Hispanic or Latino	98 (80.3%)	95 (79.2%)	193 (79.8%)
Not disclosed	1 (0.8%)	3 (2.5%)	4 (1.7%)
Race [1]			
American Indian or Alaska Native	1 (0.8%)	0 (0.0%)	1 (0.4%)
Asian	4 (3.3%)	5 (4.2%)	9 (3.7%)
Black or African American	10 (8.2%)	12 (10.0%)	22 (9.1%)
Native Hawaiian or other Pacific Islander	0 (0.0%)	1 (0.8%)	1 (0.4%)
White	102 (83.6%)	93 (77.5%)	195 (80.6%)
Other	5 (4.1%)	9 (7.5%)	14 (5.8%)
BMI (kg/m^2)			
Mean (SD)	30.7 (7.3)	29.8 (6.7)	30.3 (7.0)
Median	29.6	28.7	29.2
Min, Max	18.9, 56.7	17.9, 54.1	17.9, 56.7
[1] Race reported as "Other" if more than 1 race is selected			

Table 3 - Baseline Demographics of Patients in RESET-RA Study

Medical history of prior biological and targeted synthetic DMARDs (b/tsDMARDs) is presented in **Table 4**.

	Treatment (N=122)	Control (N=120)	All (N=242)
Prior b/tsDMARDs			
Mean (SD)	2.5 (2.0)	2.7 (1.9)	2.6 (1.9)
Median	2.0	2.0	2.0
Min, Max	1.0, 12.0	1.0, 10.0	1.0, 12.0
Number of prior b/tsDMARDs			
0	0	0	0
1	52 (42.6%)	42 (35.0%)	94 (38.8%)

	Treatment (N=122)	Control (N=120)	All (N=242)
2	25 (20.5%)	28 (23.3%)	53 (21.9%)
3 or more (3+)	45 (36.9%)	50 (41.7%)	95 (39.3%)
Prior b/tsDMARD by Classification			
Anti-IL-1 agents	0 (0.0%)	4 (3.3%)	4 (1.7%)
Anti-IL-6 agents	27 (22.1%)	28 (23.3%)	55 (22.7%)
Anti-TNF agents	116 (95.1%)	109 (90.8%)	225 (93.0%)
B-cell depleting agents	13 (10.7%)	21 (17.5%)	34 (14.0%)
JAKi	25 (20.5%)	24 (20.0%)	49 (20.2%)
CTLA4-Ig	32 (26.2%)	36 (30.0%)	68 (28.1%)
Abbreviations: CTLA4-Ig, cytotoxic T-lymphocyte-associated antigen-4 immunoglobulin; IL, interleukin; JAKi, Janus kinase inhibitor; SD, standard deviation; TNF, tumor necrosis factor			

Table 4 - Baseline Prior b/tsDMARD History

Table 5 highlights the baseline disease characteristics, including components for various effectiveness outcomes such as ACR response rate, DAS28-CRP and CDAI at baseline.

	Treatment (N=122)	Control (N=120)	All (N=242)
RA duration (years)			
Mean (SD)	13.0 (10.6)	11.8 (10.4)	12.4 (10.5)
Median	10.0	8.5	9.2
Min, Max	0.1, 55.5	0.7, 51.8	0.1, 55.5
CDAI score			
Mean (SD)	36.1 (12.6)	38.2 (12.8)	37.1 (12.7)
Median	33.8	37.1	35.1
Min, Max	13.5, 73.5	16.5, 74.0	13.5, 74.0
DAS28-CRP score			
Mean (SD)	5.3 (0.91)	5.4 (0.96)	5.3 (0.93)
Median	5.2	5.3	5.3
Min, Max	3.4, 7.6	3.0, 7.9	3.0, 7.9
Serology			
Negative	56 (45.9%)	54 (45.0%)	110 (45.5%)
Positive	62 (50.8%)	66 (55.0%)	128 (52.9%)
Not Done	4 (3.3%)	0 (0.0%)	4 (1.7%)
TJC28			
Mean (SD)	14.1 (6.9)	15.0 (7.3)	14.6 (7.1)
Median	12.4	14.0	14.0
Min, Max	4.0, 28.0	4.0, 28.0	4.0, 28.0
SJC28			
Mean (SD)	9.6 (5.5)	10.5 (5.0)	10.0 (5.2)
Median	7.8	9.2	9.0
Min, Max	4.0, 28.0	4.0, 28.0	4.0, 28.0
HAQ-DI score			
Mean (SD)	1.4 (0.6)	1.3 (0.6)	1.4 (0.6)
Median	1.4	1.4	1.4
Min, Max	0.1, 2.8	0.0, 2.9	0.0, 2.9
Pain (per patient report)			
Mean (SD)	5.5 (2.0)	5.7 (2.2)	5.6 (2.1)

	Treatment (N=122)	Control (N=120)	All (N=242)
Median	5.5	6.0	6.0
Min, Max	1.0, 10.0	1.0, 10.0	1.0, 10.0
Patient Global Assessment			
Mean (SD)	6.2 (2.1)	6.0 (2.3)	6.1 (2.2)
Median	6.0	6.0	6.0
Min, Max	2.0, 10.0	1.0, 10.0	1.0, 10.0
Physician Global Assessment			
Mean (SD)	6.3 (1.9)	6.7 (1.7)	6.5 (1.8)
Median	6.3	7.0	7.0
Min, Max	1.5, 10.0	2.0, 10.0	1.5, 10.0
hsCRP (mg/L)			
Mean (SD)	8.41 (12.34)	8.01 (12.76)	8.21 (12.53)
Median	3.87	2.63	3.08
Min, Max	0.15, 69.76	0.09, 85.48	0.09, 85.48

Abbreviations: CDAI, Clinical Disease Activity Index, DAS28-CRP, Disease Activity Score using 28-joint count and C-reactive protein; Serology includes Rheumatoid Factor and/or Anti-citrullinated Protein Antibody (ACPA); TJC28, tender joint count for 28 joints; SJC28, swollen joint count for 28 joints; hsCRP, High-sensitivity C-reactive protein

Table 5 - Baseline Scores for Disease Activity and ACR Response Rate Components

Safety

Summary of safety of the SetPoint System is reported based on adverse events reporting observed during the RESET-RA study. Adverse events reported by the study doctor as related to either the implantation procedure, device or stimulation associated with the SetPoint System are summarized below.

Overall, no patients during the study experienced a life-threatening complication related to the SetPoint System, and no deaths were reported for any cause.

Summary of Adverse Events (AEs) through primary endpoint at Week 12

During the period from Screening through Week 12, non-serious AEs occurred in 13.9% of treatment and 18.3% of control patients. Most were related to the implantation procedure. The overall rate of serious adverse events (SAEs) related to the implantation procedure or SetPoint System was 1.6% based on the safety population. No events resulted in discontinuation of a patient during this period. There were no Unanticipated Adverse Device Effect (UADEs) and no deaths from Screening to Week 12. The serious adverse events related to the implantation procedure or SetPoint System during the period from implantation procedure to Week 12 are summarized in **Table 6**.

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	3 (2.5%)	1 (0.8%)
Incision site swelling [1]	1 (0.8%)	0
Vocal cord paresis [1]	1 (0.8%)	0
Dysphonia [1]	0	1 (0.8%)
Pharyngeal perforation [2]	1 (0.8%)	0

Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.
[1] Procedure-related, onset prior to randomization: incision site swelling hospitalized for evaluation that ruled out infection (resolved); vocal cord paresis with dysphagia that led to hospitalization (resolved); dysphonia deemed by investigator significant enough to impair daily activities (resolved, mild sequelae).
[2] Occurred during explant procedure, repaired intraoperatively, no hospitalization required (resolved).

Table 6 – Related, Serious AEs from Implantation Procedure to Week 12

Non-serious AEs related to the implantation procedure and/or Implant are summarized in **Table 7**. Overall, AEs related to the procedure occurred in 16% of patients. These AEs were generally mild to moderate in severity and anticipated based on the nature of the surgical intervention.

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	17 (13.9%)	22 (18.3%)
Vocal cord paresis	5 (4.1%)	6 (5%)
Dysphonia	4 (3.3%)	3 (2.5%)
Cough	1 (0.8%)	0
Diarrhea	1 (0.8%)	0
Dysphagia	1 (0.8%)	2 (1.7%)
Dyspnea	1 (0.8%)	0
Gastrointestinal complication	1 (0.8%)	0
Implant site hypoesthesia	1 (0.8%)	1 (0.8%)
Implant site inflammation	1 (0.8%)	1 (0.8%)
Implant site swelling	1 (0.8%)	2 (1.7%)
Medical device site swelling	1 (0.8%)	0
Migraine	1 (0.8%)	0
Postoperative wound infection	1 (0.8%)	0
Rash	1 (0.8%)	1 (0.8%)
Scar pain	1 (0.8%)	0
Stitch abscess	1 (0.8%)	0
Swelling	1 (0.8%)	0
Swelling of eyelid	1 (0.8%)	1 (0.8%)
Application site rash	0	2 (1.7%)
Eyelid ptosis	0	1 (0.8%)
Headache	0	1 (0.8%)
Implant site erythema	0	1 (0.8%)
Implant site pain	0	2 (1.7%)
Oropharyngeal pain	0	1 (0.8%)
Procedural pain	0	1 (0.8%)
Suture related complication	0	1 (0.8%)
Thrombophlebitis superficial	0	1 (0.8%)

Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.

Table 7 - Non-Serious Procedure or Implant Related AEs from Implant to Week 12

Stimulation therapy was well-tolerated, with all AEs reported as mild or moderate in severity (**Table 8**).

MedDRA Preferred Term	Treatment (N=122) n (%)	Control (N=120) n (%)
Patient with AE	10 (8.2%)	0
Medical device pain	4 (3.3%)	0
Choking sensation	1 (0.8%)	0
Cough	1 (0.8%)	0
Dysgeusia	1 (0.8%)	0
Oropharyngeal pain	1 (0.8%)	0
Procedural nausea	1 (0.8%)	0
Retching	1 (0.8%)	0
Toothache	1 (0.8%)	0
Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.		

Table 8 - Stimulation Related AEs from Randomization to Week 12

There was a single event of contact dermatitis from use of the Charger. This was addressed by the patient eliminating direct contact with the Charger by wearing clothing or other fabric.

Summary of Adverse Events (AEs) in Long-Term Follow-Up

During open-label, long-term follow-up, from Week 12 until the data cut date (March 10, 2025), 5% of patients in the Treatment to Open Label (TOL) population and 4.2% in the Control to Open Label (COL) population experienced an AE related to implantation procedure or SetPoint System. None of these were serious. Most were related to stimulation, and mild or moderate in severity. Two patients discontinued treatment due to non-serious, related-AEs.

There were no related-serious AEs, Unanticipated Adverse Device Effect (UADEs) or deaths reported during Long-Term Follow-up.

There was one instance of non-serious, moderate vocal cord paresis reported after Week 12. This event is classified as related to the implantation procedure. All other AEs that occurred during long-term follow-up were related to stimulation, all were mild or moderate in severity, occurred in 5% of patients overall. (**Table 9**). These AEs were addressed by adjusting strength or time of stimulation.

MedDRA Preferred Term	TOL (N=121) n (%)	COL (N=120) n (%)
Patient with AE	6 (5%)	5 (4.2%)
Poor quality sleep	2 (1.7%)	0 (0%)
Implant site paresthesia	1 (0.8%)	0 (0%)
Medical device discomfort	1 (0.8%)	0 (0%)
*Medical device site discomfort	1 (0.8%)	0 (0%)
(exacerbation of) Trigeminal neuralgia [1]	1 (0.8%)	0 (0%)
Dysphonia	0 (0%)	1 (0.8%)
*Implant site pain	0 (0%)	1 (0.8%)
Muscle spasms	0 (0%)	1 (0.8%)
Presyncope	0 (0%)	1 (0.8%)
Temporomandibular joint syndrome	0 (0%)	1 (0.8%)
Given in the table are number of patients, with percentage, experiencing events for each AE category. At each level of summation, patients are counted only once.		

MedDRA Preferred Term	TOL (N=121) n (%)	COL (N=120) n (%)
*Relationship to implant device was also indicated for these events [1] Exacerbation of neuralgic symptoms of trigeminal neuralgia		

Table 9 - Stimulation Related AEs during Long-Term Follow-up

Explant Summary

At the time of FDA review for the SetPoint System, the Implant was explanted in 14 of the 242 (5.8% patients). The average duration between implantation and explant among the 14 patients was 469 days, ranging from 141 to 1,364 days. No patients were explanted through Week 12 visit, and 1 Implant was explanted between Week 12 and Week 24 visits. The remainder were explanted after the Week 24 visit.

Effectiveness

The primary endpoint of the RESET-RA study was the proportion of patients achieving ACR20 response at Week 12 from baseline at day of informed consent. After Week 12, the study was open label, with one-way crossover of patients in the control group to the treatment group, with efficacy assessments repeated every 12 weeks. Patients were imputed as non-responder if rescued with steroids or b/tsDMARDs or if missing any data at Week 12 and excluded at all other time points.

ACR20 response at Week 12 showed a statistically significant difference between treatment and control groups (p-value=0.0209, 95% CI 0.6 to 23.1) (**Table 10**).

All Patients						
Group	Total	Number	ACR20 Response %	Difference from Control		
				Difference	95% CI for Difference	p-Value*
Treatment	122	43	35.2%	11.8%	0.6, 23.1	0.0209
Control	120	29	24.2%			
*p-value for all patients based on the Cochran-Mantel-Haenszel test accounting for stratification.						

Table 10 - ACR20 Response at Week 12 from Baseline by Intention-to-treat (ITT)

The evolution of ACR20 response rate through Week 48 is presented in **Table 11**. During Open-Label Follow-up, rates are reported as All Completers and Non-Augmented and show ACR20 response rates further improved and appear to be durable.

ACR20 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
Baseline	122	0.0% (0)	0.00	120	0.0% (0)	0.00	N/A	
0	122	4.1% (5)	0.02	120	10.8% (13)	0.03		
4	115	27.8% (32)	0.04	113	24.8% (28)	0.04		
8	118	33.9% (40)	0.04	113	26.5% (30)	0.04		
12	122	35.2% (43)	0.04	120	24.2% (29)	0.04		
Long-term Follow-up, All completers								
24	119	44.5% (53)	0.05	117	55.6% (65)	0.05	236	50.0% (118)
36	119	47.9% (57)	0.05	115	55.6% (64)	0.05	234	51.7% (121)
48	119	51.3% (61)	0.05	114	54.4% (62)	0.05	233	52.8% (123)
Long-term Follow-up, Non-augmented								
24	96	52.1% (50)	0.05	98	53.1% (52)	0.50	194	52.6% (102)
36	89	51.7% (46)	0.05	87	62.1% (54)	0.05	176	56.8% (100)

48	77	55.8% (43)	0.06	81	59.3% (48)	0.05	158	57.6% (91)

Note: Baseline/screening at time of consent, Day 0 (day of randomization); patient imputed as non-responder if rescued prior to Week 12, regardless of treatment assignment; patient imputed as non-responder if missing at Week 12. Non-augmented represents patients on SetPoint System monotherapy, without addition of b/tsDMARDs or high-dose steroid therapy.

Table 11 - Evolution of ACR20 Response Through Week 48

The benefits of the SetPoint Therapy may improve slowly over the first 24 weeks of treatment, especially among those who have had experience with multiple prior b/tsDMARDs. Long-term results suggest that the effects of SetPoint Therapy are significant and durable across the entire study population.

Although not statistically powered for the secondary endpoints, consistent trends in favor of treatment were seen across secondary endpoints at Week 12, with results further improved or maintained during Open-Label Follow-up reported from Week 24 through Week 48 as All Completers and Non-Augmented (**Table 12)**.

ACR20 Response from Day 0 by ITT – at Week 12					
Group	**n**	**% (n)**	**Difference from Control**		
			Difference	**95% CI for Difference**	**p-Value**
Treatment	122	31.1% (38)	8.0%	-3.1, 19.0	0.0797
Control	120	22.5% (27)			

ACR20 Response from Day 0 – in open label follow up						
Study Week	**TOL**		**COL**		**All Treated**	
	n	**% (n)**	**n**	**% (n)**	**n**	**% (n)**
Long-term Follow-up, All completers						
24	119	43.7% (52)	117	47.9% (56)	236	45.8% (108)
36	119	50.4% (60)	115	52.2% (60)	234	51.3% (120)
48	119	48.7% (58)	114	44.7% (51)	233	46.8% (109)
Long-term Follow-up, Non-augmented						
24	96	46.9% (45)	98	49.0% (48)	194	47.9% (93)
36	89	49.4% (44)	87	57.5% (50)	176	53.4% (94)
48	77	49.3% (38)	81	48.1% (39)	158	48.7% (77)

DAS28-CRP good/moderate EULAR response by ITT – at Week 12					
Group	**n**	**% (n)**	**Difference from Control**		
			Difference	**95% CI for Difference**	**p-Value**
Treatment	122	60.7% (74)	19.5%	7.3, 31.7	0.0048
Control	120	41.7% (50)			

DAS28-CRP good/moderate EULAR response – in open label follow up						
Study Week	**TOL**		**COL**		**All Treated**	
	n	**% (n)**	**n**	**% (n)**	**n**	**% (n)**
Long-term Follow-up, All completers						
24	118	66.1% (78)	117	70.1% (82)	235	68.1% (160)
36	114	73.7% (84)	107	75.7% (81)	221	74.7% (165)
48	117	72.6% (85)	111	76.6% (85)	228	74.6% (170)
Long-term Follow-up, Non-augmented						
24	95	73.7% (70)	98	70.4% (69)	193	72.0% (139)
36	85	75.3% (64)	82	78.0% (64)	167	76.6% (128)
48	75	77.3% (58)	79	77.2% (61)	154	77.3% (119)

DAS28-CRP response (MCID -1.2) by ITT – at Week 12			
Group	**n**	**% (n)**	**Difference from Control**

			Difference	95% CI for Difference	p-Value
Treatment	122	45.1% (55)	13.2%	1.1, 25.3	0.0528
Control	120	32.5% (39)			

DAS28-CRP response (MCID -1.2) – in open label follow up						
Study Week	TOL		COL		All Treated	
	n	% (n)	n	% (n)	n	% (n)
Long-term Follow-up, All completers						
24	118	53.4% (63)	117	59.8% (70)	235	56.6% (133)
36	114	58.8% (67)	107	62.6% (67)	221	60.6% (134)
48	117	62.4% (73)	111	60.4% (67)	228	61.4% (140)
Long-term Follow-up, Non-augmented						
24	95	60.0% (57)	98	62.2% (61)	193	61.1% (118)
36	85	61.2% (52)	82	64.6% (53)	167	62.9% (105)
48	75	66.7% (50)	79	63.3% (50)	154	64.9% (100)

HAQ-DI Response (MCID ≤ -0.22) by ITT – at Week 12					
Group	n	% (n)	Difference from Control		
			Difference	95% CI for Difference	p-Value
Treatment	122	45.9% (56)	9.0%	-3.3, 21.4	0.0797
Control	120	36.7% (44)			

HAQ-DI Response (MCID ≤ -0.22) – in open label follow up						
Study Week	TOL		COL		All Treated	
	n	% (n)	n	% (n)	n	% (n)
Long-term Follow-up, All completers						
24	119	53.8% (64)	117	61.5% (72)	236	57.6% (136)
36	118	57.6% (68)	115	58.3% (67)	233	57.9% (135)
48	119	55.5% (66)	113	59.3% (67)	232	57.3% (133)
Long-term Follow-up, Non-augmented						
24	96	58.3% (56)	98	63.3% (62)	194	60.8% (118)
36	89	59.5% (53)	87	58.6% (51)	176	59.1% (104)
48	77	53.2% (41)	80	61.2% (49)	157	57.3% (90)

Table 12 - Secondary Efficacy Endpoints at Week 12 and Through Week 48

Table 13 and **Table 14** present mean changes in tender and swollen joint counts from baseline of 14.6 tender joints, and 10 swollen joints (based on 28 joint count) through Week 48.

TJC Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)		
	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD
0	122	-0.4	6.14	120	-1.2	6.47	N/A		
4	116	-5.3	7.38	113	-3.5	8.35			
8	118	-6.1	7.54	113	-3.9	7.85			
12	116	-6.3	8.15	114	-4.3	9.2			
Long-term Follow-up, All completers									
24	119	-7.4	7.63	117	-7.9	9.26	236	-7.6	8.46
36	118	-7.6	7.99	114	-8.8	8.98	232	-8.2	8.50
48	119	-7.9	8.28	114	-8.0	9.12	233	-7.9	8.70
Long-term Follow-up, Non-augmented									
24	96	-8.2	7.75	98	-8.1	9.42	194	-8.14	8.61
36	88	-7.4	7.62	87	-9.9	8.94	175	-8.6	8.37
48	77	-8.3	7.82	80	-9.0	9.24	157	-8.7	8.55

Table 13 - Mean Change in Tender Joint Count for 28 Joints (TJC28) From Baseline Through Week 48

SJC Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)		
	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD	n	Mean Change From Baseline	SD
0	122	-0.7	4.53	120	-1.0	4.86	N/A		
4	116	-3.8	5.46	113	-2.8	5.8			
8	118	-4.7	5.79	113	-3.2	5.53			
12	116	-4.4	5.99	114	-3.3	5.59			
Long-term Follow-up, All completers									
24	119	-5.4	6.35	117	-5.7	5.93	236	-5.5	6.14
36	118	-5.7	6.03	114	-6.3	6.27	232	-6.0	6.14
48	119	-5.2	7.07	114	-6.5	5.88	233	-5.8	6.53
Long-term Follow-up, Non-augmented									
24	96	-5.7	6.23	98	-5.5	5.82	194	-5.6	6.02
36	88	-5.6	5.31	87	-6.7	6.19	175	-6.1	5.77
48	77	-5.9	6.14	80	-6.7	5.76	157	-6.3	5.94

Table 14 - Mean Change in Swollen Joint Count For 28 Joints (SJC28) From Baseline Through Week 48

The evolution of proportion of patients with CDAI<10 and DAS28-CRP<3.2, representing patients in low disease activity (LDA) or remission, from randomization through Week 48 is presented in **Table 15** and **Table 16**, respectively.

CDAI < 10 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
0	122	0.8% (1)	0.01	120	4.2% (5)	0.02	N/A	
4	115	18.3% (21)	0.04	113	8.0% (9)	0.03		

CDAI < 10 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
8	118	19.5% (23)	0.04	113	11.5% (13)	0.03		
12	120	23.3% (28)	0.04	119	16.0% (19)	0.03		
Long-term Follow-up, All completers								
24	119	27.7% (33)	0.04	117	30.8% (36)	0.04	236	29.2% (69)
36	117	33.3% (39)	0.04	114	35.1% (40)	0.04	231	34.2% (79)
48	118	39.8% (47)	0.05	114	36.0% (41)	0.04	232	37.9% (88)
Long-term Follow-up, Non-augmented								
24	96	34.4% (33)	0.05	98	31.6% (31)	0.05	194	33.0% (64)
36	87	39.1% (34)	0.05	87	40.2% (35)	0.05	174	39.7% (69)
48	76	47.4% (36)	0.06	81	40.7% (33)	0.05	157	43.9% (69)

Table 15 - Evolution of CDAI LDA or Remission Rates Through Week 48

DAS28-CRP ≤3.2 Study Week	Treatment to TOL			Control to COL			All Treated (after crossover)	
	n	% (n)	SE	n	% (n)	SE	n	% (n)
0	122	1.6% (2)	0.01	117	4.3% (5)	0.02	N/A	
4	115	16.5% (19)	0.03	113	8.0% (9)	0.03		
8	117	17.9% (21)	0.04	113	10.6% (12)	0.03		
12	119	26.1% (31)	0.04	119	15.4% (18)	0.03		
Long-term Follow-up, All completers								
24	118	30.5% (36)	0.05	117	31.6% (37)	0.05	235	31.1% (73)
36	114	33.3% (38)	0.04	107	37.4% (40)	0.05	221	35.3% (78)
48	117	42.7% (50)	0.05	111	37.8% (42)	0.05	228	40.3% (92)
Long-term Follow-up, Non-augmented								
24	95	36.8% (35)	0.05	98	32.6% (32)	0.05	193	34.7% (67)
36	85	36.5% (31)	0.05	82	42.7% (35)	0.05	167	39.5% (66)
48	75	49.3% (37)	0.06	79	40.5% (32)	0.06	154	44.8% (69)

Table 16 - Evolution of DAS28-CRP LDA or Remission Rates Through Week 48

The Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) is validated for hand-MRI. RAMRIS measures of inflammation and structural damage also correlate independently with physical function, pain and patient global assessments, with improvements in synovitis and bone erosion associated with improvements in patient reported outcomes. Early MRI erosion progression at 12 weeks is a sensitive predictor of structural damage at 1 year. MRI erosion progression (change > 0.5 in RAMRIS erosion score) by Week 12 is associated with higher disability at 2 years (HAQ), mirroring characteristics of those with 1-year x-ray progression (Ann Rheum Dis. 2017;76(6):992-997; Ann Rheum Dis. 2014;73(11):1968-1974).

In the ITT population, 216 patients had RAMRIS scores measured at baseline and Week 12 (treatment 109, control 107). Prespecified subgroup analyses included patients with an Erosive Phenotype (treatment 57, control 48), defined as synovitis score of 2 or more on any individual joint, at least 4 joints with a score of 1, or any joint with osteitis at baseline, as well as those that had failed only 1 prior b/tsDMARD (46 treatment, 36 control).

The proportion of bone erosion progressors by all patients and the subgroups of Erosive Phenotype and 1 prior b/tsDMARD are shown in **Table 17**.

Subgroup	n	Treatment % (n)	SE	n	Control % (n)	SE	p-value
All	108	16.7% (18)	0.04	105	20.0% (21)	0.04	0.2476
Erosive Phenotype	53	18.9% (10)	0.05	45	37.8% (17)	0.07	0.0156
1 b/tsDMARD	46	6.5% (3)	0.04	36	25% (9)	0.07	0.0099

Table 17 - Proportion of Bone Erosion Progressors (>0.05 Change in Erosion Score) from Baseline to Week 12 in All Patients and Subgroup of Erosive Phenotype

The mean score changes in bone erosion, synovitis and osteitis from baseline to Week 12 among all patients, patients and the subgroups is presented in **Table 18**.

Mean Change in Erosion Score at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.2	0.85	0.08	105	0.5	1.74	0.17	0.0618
Erosive Phenotype	53	0.3	1.09	0.15	45	1.1	2.51	0.37	0.0156
1 b/tsDMARD	46	0.0	0.60	0.09	36	0.8	2.57	0.43	0.0441
Mean Change in Synovitis Scores at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.0	1.64	0.16	105	0.1	1.51	0.15	0.2871
Erosive	53	-0.1	2.27	0.31	45	0.0	1.77	0.26	0.4345
1 b/tsDMARD	46	0.1	0.81	0.12	36	0.6	1.78	0.30	0.0900
Mean Change in Osteitis Scores at Week 12									
Subgroup	**n**	**Treatment**	**SD**	**SE**	**n**	**Control**	**SD**	**SE**	**p-value**
All	108	0.1	2.61	0.25	104	0.8	4.13	0.40	0.0662
Erosive	53	0.2	3.74	0.51	45	1.8	6.18	0.92	0.0450
1 b/tsDMARD	46	-0.3	2.22	0.31	36	1.1	4.92	0.82	0.0350

Table 18 - Mean Change in Erosion, Synovitis and Osteitis Scores at Week 12

Continuation of treatment with the SetPoint System was assessed at Week 24, 36 and 48 to evaluate Therapy Persistence. Therapy Persistence on stimulation therapy, and Therapy Persistence on Setpoint System alone (non-augmented) are summarized in **Table 19**.

Persistence	Week 24			Week 36			Week 48		
	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)
Yes: SetPoint as standalone therapy *(no augmentation)*	78.7% (96)	82.5% (99)	80.6% (195)	73.0% (89)	73.3% (88)	73.1% (177)	63.1% (77)	67.5% (81)	65.3% (158)
Yes: Augmentation *(SetPoint with b/tsDMARD additional csDMARD and/or steroid added after Week 12)*	19.7% (24)	15.8% (19)	17.8% (43)	25.4% (31)	23.3% (28)	24.4% (59)	35.2% (43)	29.2% (35)	32.2% (78)

Persistence	Week 24			Week 36			Week 48		
	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)	Treatment (N=122) % (n)	Control (N=120) % (n)	All (N=242) % (n)
Augmentation with b/tsDMARD	13.9% (17)	10.0% (12)	12.0% (29)	20.5% (25)	18.3% (22)	19.4% (47)	26.2% (32)	23.3% (28)	24.8% (60)
Augmentation with additional csDMARD and/or steroid	7.4% (9)	6.7% (8)	7.0% (17)	5.7% (7)	7.5% (9)	6.6% (16)	13.1% (16)	10.0% (12)	11.6% (28)
Yes: SetPoint as standalone or augmentation therapy	98.4% (120)	98.3% (118)	98.3% (238)	98.4% (120)	96.7% (116)	97.5% (236)	98.4% (120)	96.7% (116)	97.5% (236)
No: VNS suspended, or device removed	1.6% (2)	1.7% (2)	1.7% (4)	1.6% (2)	3.3% (4)	2.5% (6)	1.6% (2)	3.3% (4)	2.5% (6)

Table 19 - Persistence with SetPoint Therapy (based on ITT)

Patient satisfaction was assessed at Week 24 using five-point Likert rating scale. Additionally, patients were asked a question about whether they would recommend the SetPoint System to family and friends (**Table 20**).

	TOL [1] (N=122)	COL [2] (N=120)	All (N=242)
How satisfied are you with the SetPoint System for treatment of RA?			
N [3]	119	114	233
Somewhat to very satisfied	90 (75.6%)	92 (80.7%)	182 (78.1%)
Neither satisfied nor dissatisfied	14 (11.8%)	12 (10.5%)	26 (11.2%)
Somewhat to very dissatisfied	15 (12.6%)	10 (8.8%)	25 (10.7%)
Would you recommend the SetPoint System to a family member or a friend?			
N [3]	118	114	232
Yes	108 (91.5%)	110 (96.5%)	218 (94.0%)
No	10 (8.5%)	4 (3.5%)	14 (6.0%)

Abbreviations: COL, Control to Open Label; TOL, Treatment to Open Label
[1] Treatment to Open Label (TOL): The TOL population comprises treatment patients from ITT population who received active stimulation through Week 12, completed Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[2] Control to Open Label (COL): The COL population comprises Control patients from ITT population who received non-active (sham) stimulation through Week12, switched to active stimulation after completing Week 12 assessments, continued to receive active stimulation during open-label follow-up, and for whom follow-up data are available.
[3] Percentage calculated based on each analysis population (i.e., TOL, COL).

Table 20 - Patient Satisfaction and Recommendation at Week 24