The Genio® System 2.1
Patient Manual

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

Patented and design protected technology.

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Contact Information

During the activation visit, fill in the contact information below.

Health Care Provider

Name:	
Phone Number:	

Implanting Hospital

Name:	
Address:	
Surgeon Name:	
Surgeon Phone Number:	

Users, Family Members and Caregivers

Important Information:

- You should read this manual carefully before you start using the Genio® System 2.1. If you have any questions or problems, refer to the “Troubleshooting” section. If your questions are not answered in this patient manual, please contact your health care provider.
- Always have your Implant Card with you and inform your health care providers that you have been implanted with the Genio® System 2.1 in the chin area. If they have any questions, your health care providers can contact Nyxoah at the number provided on page 2.
- If you experience any unusual symptoms or problems related to the use of your Genio® System 2.1, report this to your health care provider at your earliest convenience. Refer to the Contact Information section (on previous page).

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Glossary

Genio® Activation Chip (Activation Chip or AC), Model #2364 – The part of the Genio® System 2.1 which contains the battery and the customized therapy program.

Apnea – A temporary absence of breathing during sleep.

Apnea-Hypopnea Index (AHI) – A measurement of the severity of a person's sleep apnea based on the number of times the patient pauses breathing while asleep.

Atrial Fibrillation – A type of abnormal heartbeat.

Body Mass Index (BMI) – A measure that uses your height and weight to work out if your weight is healthy.

Caution – A statement describing actions that may result in minor or moderate injury to the patient, device damage or improper functioning of the device.

Central Apnea – A temporary absence of breathing without effort to breathe.

Genio® Charging Unit (Charging Unit), model #2238 – The part of the Genio® System 2.1 that recharges the battery of the Activation Chip.

Contraindication – A condition or situation when the Genio® System 2.1 should not be used.

Customized Therapy Program – The personalized stimulation settings stored in the Genio® Activation Chip that defines the therapy delivered by the Genio® System 2.1.

Defibrillation/Cardioversion – The use of electricity to treat an abnormal heart rhythm**.**

Delay Time – The time that allows the patient to fall asleep before the device starts working.

Diathermy – A medical treatment that uses electric current to generate heat in the body. This treatment is typically used to relieve pain, stiffness and muscle spasms, reduce joint contractures (in other words, shortening of muscles or tendons), reduce swelling and pain after surgery, and promote wound healing.

Genio® Disposable Patch (Disposable Patch) – The part of the Genio® System 2.1 which allows stimulation to flow from the Activation Chip to the Implantable Stimulator.

Drug-Induced Sleep Endoscopy (DISE) – Procedure performed under sedation during which an endoscope (thin flexible tube with a camera) is used to visualize the site of collapse at different levels of the upper airway. This exam helps identify potential blockage of breathing in the upper airways that may be contributing to the patient's snoring and sleep apnea.

Electrode – The conductive part of the Implantable Stimulator that allows stimulation energy to flow to the hypoglossal nerve.

Genio® System 2.1 – The system developed by Nyxoah to treat Obstructive Sleep Apnea.

Hyperbaric Chamber – A special chamber or compartment in which pure oxygen is delivered to a person under very high pressure and is used for some medical treatments.

Hypoglossal Nerve – The nerve that controls tongue movement.

Hypopnea – An abnormal slow or shallow breathing.

Indication – A medically proven clinical reason to use the Genio® System 2.1.

Genio® Implantable Stimulator (Implantable Stimulator or IS) – The part of the Genio® System 2.1 consisting in a small device implanted in the chin area close to tongue muscle nerves, that contains electronics that control the stimulation.

Lithotripsy – A medical procedure that uses shock waves or lasers to break down stones in the kidneys, bladder, or ureter.

Magnetic Resonance Imaging (MRI) – A non-invasive diagnostic technique for producing images of internal body tissues.

Mixed Apnea – A temporary absence of breathing with partial effort to breathe.

MR Conditional – a medical device with demonstrated safety in the MR environment within defined conditions.

Obstructive Sleep Apnea (OSA) – A common type of sleep apnea caused by obstruction of the upper airway.

Pause – A temporary suspension of stimulation.

Positive Airway Pressure (PAP) — A common treatment for obstructive sleep apnea. PAP devices provide patients with a stream of compressed air while they sleep to keep the airway open. Examples include CPAP and BiPAP.

Precaution – See caution.

Radiation Therapy – An ionizing energy commonly used to treat cancer.

Radio-Frequency or Microwave Ablation – Treatments that use heat to destroy cancer cells.

Sleep Study – An overnight evaluation of your sleep apnea. Stimulation settings may be adjusted during a sleep study.

Genio® Smartphone Application – An optional application that is loaded onto your smartphone to allow you to pause and resume treatment, and to fine tune the stimulation parameters within a pre-defined limit.

Stimulation – The delivery of small electrical pulses to the hypoglossal nerve by the Genio® System 2.1.

Ultrasound – Sound waves with frequencies higher than the upper audible limit of human hearing.

Upper Airway – The breathing path from the mouth and nostrils to the larynx (vocal cords).

Ventricular Fibrillation – An abnormal heartbeat that can be life-threatening.

Warning – A statement describing an action or situation that could seriously harm the patient.

About this User Guide

You have received this manual because you have been implanted with a Genio® Implantable Stimulator to treat moderate to severe Obstructive Sleep Apnea (OSA).

By now, you should have healed from the surgical procedure and received a Patient Kit including Disposable Patches, an Activation Chip and a Charging Unit.

This patient manual contains important safety information. This guide also describes the Genio® System 2.1 components, how to set them up and how to use the Genio® System 2.1 once your therapy is turned on.

If you have questions that are not addressed in this patient manual, or if any unusual situations or problems occur, contact your health care provider.

1. Introduction

1.1. About Sleep Apnea

Sleep apnea is a respiratory disorder caused by episodes of varying degrees of upper airway obstruction which is type of blockage of the airway that prevents breathing while sleeping. Because you may not receive enough oxygen while you sleep if you have sleep apnea, it may result in excessive daytime sleepiness and other symptoms. The most common type of sleep apnea is obstructive sleep apnea, which is caused by decreased muscle strength in the wall of the throat and tongue. As tongue and airway muscles become weaker, the upper airway is not as open, leading to decreased respiration and oxygen levels in the blood.

1.2. About Your Genio® System 2.1

1.2.1. Indications for Use

The Genio® System 2.1 is indicated for use in the treatment of moderate to severe Obstructive Sleep Apnea (OSA) (apnea-hypopnea index [AHI] of greater than or equal to 15 and less than or equal to 65). The Genio® System 2.1 is intended for adults 22 years of age and older who have been confirmed to fail, cannot tolerate or are ineligible to be treated with current standard of care treatments including lifestyle modifications, positive airway pressure (PAP) treatments (such as continuous positive airway pressure [CPAP] or bi-level positive airway pressure [BiPAP] machines, oral appliances (such as mandibular advancement devices), and pharmacotherapy (such as tirzepatide).

PAP failure is defined as an inability to eliminate OSA (AHI of greater than 15 despite PAP usage), and PAP intolerance is defined as:

1. Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night), or
2. Unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it).

1.2.2. System Overview

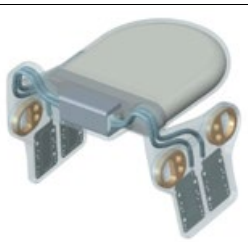
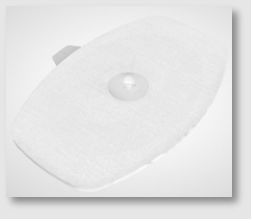
The Genio® Implantable Stimulator is surgically implanted in your chin area. After a healing period, you attend sleep lab sessions where instructions tailored to your sleep needs are programmed into an Activation Chip. You will charge the Activation Chip daily using its Charging Unit.

Prior to going to sleep, you connect your fully-charged Activation Chip to a Disposable Patch and apply the Disposable Patch to your chin. After a delay period to allow you to fall asleep, the Activation Chip sends stimulation energy pulses to your implant according to the instructions that were programmed during the sleep lab session. In the morning, you remove the Disposable Patch to stop stimulation and return the Activation Chip to its Charging Unit.

You can control your treatment and view usage data using the optional Genio® Smartphone Application.

1.3. Genio® System 2.1 Components

Your Genio® System 2.1 is made up of four main parts: The Implantable Stimulator, Activation Chip, Charging Unit and the Disposable Patch. Here is what each part of the system does:

The **Implantable Stimulator** is a small saddle-shaped implant. It has a flat area, which encloses an antenna and two "legs" with two metal pads each, called electrodes. It is surgically implanted under the chin, close to a nerve in the tongue called the hypoglossal nerve. The electrodes conduct stimulation energy to the hypoglossal nerve, resulting in contraction of tongue muscles. This process can help maintain an open airway and normalize breathing during sleep.	
The **Activation Chip** assembly contains a programmable chip and a battery. The battery provides power to the Implantable Stimulator. The chip is programmed with the settings that provide the stimulation therapy that your health care provider has chosen for you and has a battery. You will be required to charge the Activation Chip daily. The Activation Chip comes with a cover to protect it when it is not in use or being charged. The Activation Chip can be controlled by an optional Smartphone Application, designed to operate on both Android and iOS devices. The Smartphone App allows you to pause and resume stimulation and adjust your treatment amplitude within a pre-defined range.	
The **Charging Unit** and its power adapter are used to recharge the Activation Chip's battery.	
The **Disposable Patch** is an adhesive patch placed on the skin under the chin. The Disposable Patch is snapped onto the Activation Chip. Once snapped together stimulation energy can be transmitted to the Implantable Stimulator.	

A summary of the technical specifications for each of the physical Genio® System 2.1 components (i.e., components that are not software) which you will use is provided in the table below.

Component	Dimensions	Weight	Shelf-life	Service Life	Temperature Limitations
Implantable Stimulator Model #2954	L=27.3mm W=20.7mm H=4.4mm	6.18g	2 years	At least 12 years	Storage: 59°F - 81°F
Disposable Patch (liner included)	L=101mm W=71.7mm H=6.61mm	3.25g	- Sealed bag: Maximum 16 months - Opened bag: 15 days	N/A – single use disposable device	Storage: 59°F - 81°F
Activation Chip Model #2364	Ø = 31.40mm H=20.55mm	12.18g	1 year	At least 12 months	Storage: 59°F - 81°F Operating: < 102.2°F
Charging Unit Model #2238	L=110mm W=50mm H=17mm	61.69g	1 year	At least 12 months	Storage: 59°F - 81°F

Another important component of your system is your implant card. This card supplies information about your Genio® System 2.1 and your health care provider contact information. Keep your Implant Card with you at all times. In case of a medical emergency or if you need to bypass security, present this card to security or medical personnel.

2. Safety Information

2.1. Contraindications

The Genio® System is contraindicated for:

- Patients with combined central and mixed apnea-hypopnea index greater than or equal to 25% of the total AHI
- Patients with any functional or structural problem, medical illness or condition that would prevent or interfere with implantation, activation or continued use of the Genio therapy
- Patients with an implantable device which may be susceptible to unintended interaction with the Genio® System. Consult the device manufacturer to assess the possibility of interaction.
- Women who are pregnant, planning to become pregnant or breastfeeding.
- Any condition or procedure that has compromised neurological control of the upper airway.

2.2. Warnings

2.2.1. Patient Population

Safety and effectiveness in the following groups have not been established with the Genio® System 2.1:

- Patients below 22 or above 75 years of age
- Patients with a Body Mass Index (BMI) above 32 kg/m^2
- Patients with an Apnea Hypopnea Index (AHI) below 15 or over 65 events/hr
- Patients with Complete Concentric Collapse (CCC) at the soft palate level

2.2.2. Pregnancy

If you become pregnant while implanted with the Genio® Implantable Stimulator, discontinue use and consult your health care provider.

2.2.3. Medical Treatments

Some medical treatments may interfere with or damage your Genio® Implantable Stimulator or your body tissue.

You should consult your health care provider before undergoing any of these treatments:

- Treatment of muscle and joint conditions using heating of the tissue by high frequency electric current (diathermy)
- Radiation therapy
- Kidney stone treatment using ultrasound (lithotripsy)
- Magnetic stimulation (e.g., transcranial magnetic stimulation), or any other form of electrical stimulation (e.g., transcutaneous electrical nerve stimulations (TENS))
- Therapeutic ultrasound
- Treatments that use heat to destroy cancer cells (radiofrequency or microwave ablation)
- Treatment in a hyperbaric chamber
- Any medical treatments that involve the neck (this includes any cosmetic procedures involving the neck)

If you require any of these treatments, contact the healthcare provider overseeing your sleep care both before and after your treatment.

After the treatment, your health care provider should confirm that your Implantable Stimulator is working as intended.

2.2.4. Dental and Surgical Procedures

Ask your health care provider to avoid surgical procedures that involve the floor of the mouth or lower jaw as this could displace your implant, including:

- Injections to the floor of the mouth, and
- Use of retractors or other instruments that might put pressure on or lacerate the floor of the mouth mucosa

2.2.5. Magnetic Resonance (MR) Scan Safety

Your Genio® System 2.1 is MR Conditional and eligible for MRI scanning under certain conditions. You should inform a healthcare professional of your Implantable Stimulator prior to undergoing an MR scan.

Your Implant Card identifies your implanted device and provides the website which contains information on how to perform safe MR scans with your device (geniosleep.com/en/mri). Bring your Implant Card to every appointment, including your MR scan, so that your health care provider can assess your eligibility and obtain instructions on the MR scan limitations of your device.

2.2.6. Entering Areas with Strong Magnetic or Electric Fields

You should avoid entering any areas where strong magnetic or electric fields are present such as those with posted warning signs prohibiting or limiting access for people with AIMDs (e.g., a pacemaker). Exposure to these types of strong fields could potentially damage your Implantable Stimulator and lead to device functionality issues such as unintended stimulation.

If you are required to enter one of these areas – for example, as part of your job – you should consult with a healthcare provider to obtain their approval prior to doing so.

2.2.7. Excessive Force, Physical Activities and Sports

Excessive, repeated or prolonged outside force to the neck near your Genio® Implantable Stimulator (such as motor vehicle accident, repeatedly manipulating your neck close to the incision, certain sports or physical activities, etc.) may damage the implant and could lead to migration, loss of therapy or tissue damage.

- Avoid any activities that involve manipulation or force to the neck such as jackhammering, mixed martial arts, Brazilian jiu-jitsu, wrestling, extreme sports, etc.
- Avoid any activities that could have significant stress on the neck such as diving, boxing, bumper cars etc.
- The impact of pressure changes which could be encountered during scuba diving have not been evaluated and this activity should be avoided.

If you are involved in a motor vehicle accident or any other physical activities or sports in which you sustain excessive force to the head or neck, your health care provider should confirm that your Implantable Stimulator is still working as intended.

2.2.8. Aircraft Safety

Do not use your Genio® System 2.1 during aircraft take-off and landing. Ground radars may interfere with the Genio® System's proper operation and cause it to malfunction.

2.3. Precautions

2.3.1. Components

- Do not use any components other than those supplied by Nyxoah for the Genio® System 2.1
- Use only the power adapters provided by Nyxoah. Use of other adapters may damage the device

2.3.2. Defibrillation/Cardioversion

The possible interaction between the Genio® System 2.1 and cardiac devices (implantable defibrillators) has not been investigated. After defibrillation or cardioversion, your health care provider should confirm that the Genio® Implantable Stimulator is working as intended.

2.3.3. Implantable Cardiac Devices

If you have a Genio® Implantable Stimulator and your Cardiologist recommends a pacemaker or other implantable cardiac device (e.g., implantable cardioverter-defibrillator), ensure you tell them about your existing device. You should also inform the health care provider overseeing your sleep care about any upcoming procedures. Tongue, Lip or Cheek Piercings

If you have any type of tongue, lip or cheek piercing(s), you should remove your piercing(s) prior to nightly use of the Genio® System 2.1. Due to the tongue movement which occurs during stimulation, the presence of a tongue, lip or cheek piercing during active therapy could result in tooth injury, tongue lacerations, tongue abrasions, or injury to the floor of the mouth. You do not need to remove your piercing(s) when you are not actively using the Genio® System 2.1.

2.3.4. Oral/Dental Appliances

You may continue to use oral devices such as oral appliances, bite guards, retainers, etc. with your Genio® System 2.1 provided that such devices do not restrict tongue motion. Use of certain oral devices during active therapy may cause tongue irritation, injury, or discomfort. If you experience any of these symptoms, you should discontinue use of the oral device and contact your healthcare provider.

2.3.5. Neck Braces

Use of a neck brace with the Genio® System 2.1 could potentially interfere with the position or connection of the AC resulting in inability to effectively receive therapy or potential patient discomfort. If you are currently utilizing a neck brace, you should discontinue use of the Genio® System 2.1 until your neck issues have resolved and you have been cleared by a healthcare provider to resume Genio® therapy.

2.3.6. Security Screening Devices

Interactions with security screening devices such as metal detectors, theft detectors and RFID systems (commonly found in airports, libraries, department stores and government buildings) are unlikely to damage the Genio® Implantable Stimulator or cause clinically significant symptoms. However, the Implantable Stimulator contains metal parts that might possibly trigger these alarms.

When approaching these devices, show the security personnel your Implant Card and notify them that you have an implanted medical device in your chin area. Keep as far away from the screening device as possible and do not linger near or lean on these devices.

Note: Some theft detectors may not be visible.

2.3.7. Device Battery

Charge your Activation Chip daily so that it is fully charged for the next night of use.

After heavy use (500 charging and discharging cycles), the Activation Chip battery may lose up to 20% of its power. If you do not feel stimulation upon waking after treatment, contact your health care provider.

2.4. Risks

Medical treatments often cause side effects. You may have none, some or all the side effects listed below, and they may be mild, moderate, severe or serious if they lead to hospitalization. If you have any side effects, or are worried about them, consult your health care provider. Risks of using the Genio® System 2.1 can be minimized by following this manual, and by following your health care provider's instructions.

In addition to the risks described below, the device may have other risks that are currently unknown If you experience any unexpected side effects, inform your health care provider immediately.

Always tell your health care provider if you have new health issues or if other health care providers have recommended treatments for you.

If a severe side effect or reaction occurs, your health care provider may need to stop your therapy. Your health care provider will discuss the best way of managing any side effects with you. If you have any questions on these events, consult your health care provider.

2.4.1. Risks Associated with the Implantation Procedure

Implantation of the Genio® System is performed in an operating room and requires general anesthesia. As with any surgical procedure, there are risks associated with both surgery and the anesthesia which are independent of the risks associated with the Genio® System itself. If you have any concerns about these issues, you should discuss them with your health care provider.

The implantation surgery may involve the following risks:

Very common risks (which may affect more than 1 in 10 patients):

- Post-surgical mild to moderate pain, discomfort, stiffness or tenderness at the implant site
- Post-surgical mild to moderate swelling or bruising around the implant site
- Post-surgical numbness, tingling or other sensory changes related to the skin incision

Common risks (which may affect between 1 in 10 and 1 in 100 patients):

- Post-surgical discomfort
- Impaired or painful swallowing
- Impaired or painful speaking due to the procedure
- Paresthesia (sensation of tickling or itching)
- Bleeding
- Hematoma
- Pain or irritation in the throat or nasal passage from intubation
- Dry mouth
- Post-surgical hoarse voice
- Damage or trauma to nerves, blood vessels or muscles
- Local skin irritation
- Infection
- Worsening of OSA symptoms (e.g., fatigue or sleep disturbances)

Uncommon risks (which may affect less than 1 in 100 patients):

- Post-surgical headache
- (Transient) tongue weakness or soreness
- Tongue fasciculations (twitching of tongue) or spasm
- Muscle or skin tightness
- Post-surgical pain/complication due to the position on the table during the procedure (head extension, body position)
- Temporary lip weakness
- Post-surgical fever
- Superficial skin infection
- Impaired sense of taste
- Increase or decrease in size of the tongue muscle and/or fat
- Persistent pain at the implant site
- Abnormal scarring or healing problems

2.4.2. Risks Associated with the Devices and the Use of the Devices

The potential device-related adverse events are listed below:

Very common risks (which may affect more than 1 in 10 patients):

- Temporary local skin irritation
- Impaired or painful swallowing due to the device
- Discomfort or pain due to electrical stimulation
- Mouth blisters (due to tongue rubbing against teeth during stimulation)
- Mild to moderate pain, swelling, stiffness or tenderness at the implant site or with the use of the device

Common risks (which may affect between 1 in 10 and 1 in 100 patients):

- Mild tongue abrasion
- Abnormal scarring
- Tongue fasciculations (twitching of tongue)
- Dry mouth
- Temporary tongue muscle weakness or soreness
- Temporary usability or functionality issues with an external device leading to temporary delay of treatment
- Permanent usability or functionality issues with an external device leading to no therapy
- Usability or functionality issues with the implanted device
- Increased or continued snoring
- Headache or dizziness
- Fatigue or sleep disturbances, while acclimating to stimulation
- Change in salivary flow
- Clinically significant implant migration (device moving from implanted location and potential partial or complete expulsion of the device from its intended place)
- Presence of fibrosis making the removal of the Genio® Implantable Stimulator Model #2954 difficult without damaging the surrounding structures

Uncommon risks (which may affect less than 1 in 100 patients):

- Impaired sense of taste or metallic taste
- Increased acid reflux
- Increased upper airway secretions
- Paresthesia (sensation of tickling or itching)
- Pain or irritation in the throat or nasal passage
- Allergic and/or rejection response to the implanted device
- Damage to tissue (nerves, blood vessels or muscles) in contact with the implant or in the vicinity of the implant
- Damage to tissue in contact with external devices
- Persistent pain at the implant site
- Impaired or painful speaking due to the device

- Risks related to additional surgery and any unstudied potential effect
- Cellulitis at surgical site

2.4.3. Risks Associated with Revision (Repositioning or Replacement) and Explant Surgeries

If an additional surgery is performed in order to have the implant removed or replaced, the risks associated with the implantation procedure detailed above, along with some new risks, would apply to the revision surgery. The risks of revision surgery are higher because scar tissue builds up around the implanted device. Also, the risk of infection from the surgery is slightly higher. Injury to nerves, blood vessels or tissues around the implanted device could occur.

2.4.4. Risks Associated with Pregnancy and Breastfeeding

The effects of the Genio® System 2.1 on the unborn child and on the newborn are unknown. Because of this, **you cannot be implanted if you are pregnant or trying to become pregnant, or breastfeeding.**

If you become pregnant after being implanted, the device should not be used until you consult with your health care provider.

2.4.5. Risks Associated with Device Service Life

You can expect your Genio® Implantable Stimulator Model #2954 to continue working for at least 12 years. Nyxoah will provide support for your devices for as long as your Implantable Stimulator remains in place.

The risks of using your implant beyond the timeframe mentioned above include the potential for your Genio® therapy to become less effective or stop working altogether, possibly requiring supplemental therapy solutions to treat your OSA symptoms. You could also experience an allergic reaction to the materials of the device, however this risk is low. If you experience any perceived changes in your Genio® therapy, you should inform your health care provider.

2.5. Storage, Operating Handling and Transport Conditions

2.5.1. Storage Conditions

Keep external system components in a clean, dry area at a room temperature of approximately +15 °C to +27 °C / +59 °F to +81 °F.

CAUTION: Do NOT store devices in direct sunlight or near heating sources (such as a furnace or space heater).

CAUTION: Do NOT store devices in extremely humid areas or near sources of water. Exposure to water and/or humidity may cause the devices to malfunction.

CAUTION: If any of the system components were stored at conditions outside the parameters listed above, they cannot be used and should be returned to Nyxoah for inspection.

2.5.2. Operating Temperature

The Activation Chip contains an internal battery. To prevent the potential for battery overheating, the Activation Chip should only be operated at temperatures lower than 39°C/102.2°F.

CAUTION: Do NOT operate the Activation Chip at temperatures higher than 39°C/102.2°F as this could cause the battery to overheat.

2.5.3. Expiration Date

Disposable Patches should not be used after the expiration date. The expiration date is shown on the component's packaging label.

2.5.4. Handling

The components of the Genio® System 2.1 should be handled with care.

- Do not allow the metal pins at the bottom of the Activation Chip to touch any surface except for the Disposable Patch, the Charging Unit docking area or the Activation Chip protective cover.
- Do not place the devices on any metallic surfaces.
- Always leave the Activation Chip in the Charging Unit when not in use so that it will be fully charged for the next night of use.
- Make sure to close the zipper of the bag containing the new Disposable Patches to avoid any moisture/humidity that may affect the patch adhesive.
- All devices are tracked by identification numbers recorded by the hospital staff when the device is delivered to you. Therefore, **all devices should be brought back each time you visit your health care provider.**

2.5.5. Cleaning your Devices

Keep your devices in a clean environment. Keep the Activation Chip in its protective cover when it is not in use or not being charged. Do not attempt to clean the devices. If your device needs to be cleaned to work properly, contact your health care provider.

2.5.6. Traveling with your Devices

Be cautious when traveling with your devices. Follow the package and transport conditions of the different components:

- Always transport the Activation Chip in its protective cover
- Always transport Disposable Patches in original packaging when possible. If you are unable to use the original packaging, ensure that you do NOT fold the Disposable Patches during transport.

CAUTION: Do NOT fold the Disposable Patches as this could damage the internal electronics or the device or lead to difficulty in adhering the patch to the skin.

2.6. Alternative Therapies

There are several other alternatives for the treatment of individuals with obstructive sleep apnea (OSA), from lifestyle changes (e.g., weight loss and positional therapy) to PAP (positive airway pressure), oral appliances, anatomical surgery and hypoglossal nerve stimulation (HGNS).

Individuals with mild to moderate OSA often use lifestyle changes alone, PAP, mandibular advancement devices (oral appliance therapy), or anatomical surgery.

The treatment alternatives for individuals with moderate to severe OSA include: PAP, mandibular advancement devices (oral appliance therapy), use of Tirzepatide (in patients with comorbid obesity contributing to pathophysiology of their OSA), anatomical surgical treatments or HGNS treatments to enlarge the airway.

Each alternative has its own advantages and disadvantages. A patient should thoroughly discuss the risks and benefits of treatment alternatives with his/her healthcare provider to select the treatment method that best meets their needs.

3. DREAM Study Results

Nyxoah performed a clinical study (“DREAM”) to evaluate the safety and effectiveness of the Genio® System to treat adult subjects with moderate to severe Obstructive Sleep Apnea (OSA) in the US, Belgium, Germany and Australia. The results of the DREAM (Dual sided hypoglossal neRvE stimulAtion for the treatMent of obstructive sleep apnea) are summarized in the sections below. If you have any questions about the DREAM clinical study, contact your health care provider.

3.1. Device Under Test

The study was conducted using the 1st Generation model of the IS ("original IS"). Although the original IS and IS Model #2954 differ in certain characteristics, the two versions of the Genio® System 2.1 implant were considered functionally equivalent in key areas such as: electronic circuitry, stimulation parameters used, active stimulation area of the electrodes, mode of communication with the AC Model #2364, and use of external components. Based on all the non-clinical and pre-clinical testing conducted for IS Model #2954, it was concluded that the changes made for the IS Model #2954 did not impact the performance or functionality of the implant when compared to the original IS. Considering both the similarities between the original IS and the IS Model #2954 as well as the assessment of the design changes, the clinical data obtained with the original IS during the DREAM IDE study was considered leverageable for the IS Model #2954. An assessment of the impact any differences between the two implant models may have on the applicability of the data gathered during the DREAM clinical study has been provided in Table 1.

Table 1. Comparison of the Genio® System 2.1 Implant Used in the DREAM Clinical Study ("Original IS") and the IS Model #2954

Characteristic	Differences Between the Version of the Implant Used for the Clinical Study (Original Implantable Stimulator) and the Implantable Stimulator Model #2954	Impact of Implantable Stimulator Model #2954 Differences on Clinical Data Collected Using the Original Implantable Stimulator
Materials of construction	While there are minor differences in the materials of construction used for both versions of the implant (e.g., ceramic main body in the Implantable Stimulator Model #2954 versus Parylene coated PEEK frame in the original Implantable Stimulator), the materials with direct patient contact are the same (silicone and platinum electrodes)	No impact – the differences in the non-patient contacting materials of the original Implantable Stimulator and the Implantable Stimulator Model #2954 do not introduce were found to not pose any biological safety risks to the patient or user Results from the biocompatibility testing showed that the Implantable Stimulator Model #2954 is biologically safe to use as intended.
Thickness of main body	The main body of the Implantable Stimulator Model #2954 is slightly thicker (~1.0mm) than the original IS due to the introduction of the ceramic pouch	No impact – as the adjacent muscles (Geniohyoid and Genioglossus) are flexible, they would not be impacted by any additional thickness of the implant's main body. Results of the chronic animal study served to confirm the increase in thickness did not impact the position of the implant over time.
Number of shoulders	The number of shoulders was reduced for the Implantable Stimulator Model #2954 from a double-shoulder to a single-shoulder design	No impact – the reduction of the number of shoulders (two to one) for Implantable Stimulator Model #2954 has led to an increase in the flexibility of the paddles' connective shoulders. As the electrode positioning and suturing of the paddles remains the same, the increased flexibility of the decouples the forces generated from main body movement and the forces pulling the paddles sutures, thus there would be no impact on the mechanical interface of the paddle with the nerve (i.e., no change to the clinical effects). Changes to a single shoulder design allows for easier handling and positioning of the paddles over the HGN during the implantation procedure. Results from the HF validation study done for the Implantable Stimulator Model #2954 showed that there was no impact to the ability to correctly perform the implantation procedure or properly position the implant due to the reduction of shoulders.
Width/thickness of paddle shoulders from top view at maximal height	The width/thickness of the Implantable Stimulator Model #2954 paddle shoulders (~3.15mm one shoulder width/thickness) is slightly greater than the original Implantable Stimulator (~2.48mm/2.60mm for one shoulder or ~4.96mm/5.2mm for both shoulders)	No impact – while the width/thickness of the paddle shoulders of the Implantable Stimulator Model #2954 is slightly larger for one shoulder versus the two for the original Implantable Stimulator, the difference is considered negligible relative to the change from a two-shoulder design in the original Implantable Stimulator versus a single shoulder design in the Implantable Stimulator Model #2954 (as described above).
Average total mass	The mass increased from 3.0g to 6.15g in the Implantable Stimulator Model #2954	No impact – the paddles of the Implantable Stimulator Model #2954 are sutured into place like they are for the original Implantable Stimulator while fibrosis occurs which will further help to maintain positional stability of the implant. The positional stability of the main body of the Implantable Stimulator Model #2954 prior to fibrotic tissue

Characteristic	Differences Between the Version of the Implant Used for the Clinical Study (Original Implantable Stimulator) and the Implantable Stimulator Model #2954	Impact of Implantable Stimulator Model #2954 Differences on Clinical Data Collected Using the Original Implantable Stimulator
		formation was verified as part of chronic animal study. Results of the study showed that there was no impact to the position of the implant over time due to the increase in mass. Additionally, the Implantable Stimulator Model #2954 has increased flexibility of the connecting shoulders which reduces the exertion forces on the paddle sutures, the interface of the electrode with the HGN would not be expected to change over time due to the increase in implant mass. The reduction of forces exerted on the suturing anchors due to increase of shoulder flexibility was confirmed through a dedicated Finite Element Analysis (FEA) comparison and associated bench testing. The FEA assessed the susceptibility of paddle migration under extreme physiological loading modes both with and without fibrotic tissue. Suturing scenarios (including simulated suture rupture) were verified by supportive bench testing. Stresses and forces were evaluated for both the original Implantable Stimulator and Implantable Stimulator Model #2954. Results of the FEA and bench testing showed that due to the design changes made for the Implantable Stimulator Model #2954, the forces exerted on the suturing anchors due to implant body movement were equal to or lower than the original Implantable Stimulator across all displacement ranges, even with one suturing anchor unsecured. These tests serve to support that despite an increase in mass, there is no increase in the potential risk of migration of the Implantable Stimulator Model #2954 when compared to the original Implantable Stimulator.
Expected service life	The expected service life of the Implantable Stimulator Model #2954 increased to 12 years from three (3) years in the original Implantable Stimulator due to the introduction of the hermetic ceramic enclosure used for the main body	No impact – the increase in device lifetime means the Implantable Stimulator Model #2954 will need to be replaced less often. This difference does not impact the results of the clinical study.

While the clinical data obtained with the original Implantable Stimulator during the DREAM study is considered leverageable for the Implantable Stimulator Model #2954, there are two key limitations to using data from the original Implantable Stimulator to support the newer Implantable Stimulator Model #2954:

1) The method relies on empirical observations to infer the performance of an untested device in human subjects, and
2) The introduction of new design variables, although potentially enhancing performance, does not allow for a direct comparison of the two designs.

Therefore, the Implantable Stimulator Model #2954 will be further evaluated as part of the Genio® System 2.1 post-approval study.

3.2. Patients Studied

Between October 14, 2020 and March 3, 2023, the study enrolled 687 participants. These participants were evaluated against predefined patient selection criteria, which included adults with moderate to severe OSA that had failed or not tolerated Positive Airways Pressure (PAP) treatments, having a BMI less than or equal to 32, without complete concentric collapse (CCC) at the soft palate level (evaluated by performing a Drug Induced Sleep Endoscopy [DISE]). A total of 568 subjects did not meet these criteria; 2 patients were not implanted due to study enrollment closing, and 2 other patients were not implanted due to lack of site staff resources. Implant was attempted in a total of 115 subjects with 113 of them being successfully implanted with the Genio® system. The results were analyzed in all 115 patients (Intent-To-Treat, ITT population) and in 110 patients (modified Intent-To-Treat, mITT population) that successfully completed the implant procedure. An additional 3 patients were also not included because their data was unmonitored. A total of 88 patients completed the 12 months without major (critical) deviations (Per-Protocol population). All patients that did not have results at 12 months were treated as non-responders.

Table 2 summarizes the patient demographics for the study.

Table 2. Patient Demographics

Demographic / Participant Characteristics	Mean ± SD (N = 115)	Median (Min; Max)
Age, year	56.8 ± 7.3	57 (36;71)
Male, gender	70.4% (81/115)	
Body Mass Index, kg/m^2	28.50 ± 2.63	28.7 (21.7; 32.0)
BP Systolic, mmHg	132.6 ± 16.5	131
BP Diastolic, mmHg	79.9 ± 10.0	80
Neck Circumference, cm	40.55 ± 5.73	40.6 (30.5; 86.4)
Race: Caucasian	93.9% (108/115)	NA
Race: Asian	0.9% (1/115)	NA
Race: Black or African American	3.5% (4/115)	NA
Race: Other	1.7% (2/115)	NA
OSA Characteristics	**Mean ± SD (N = 110)**	
AHI events/h	28.00 ± 11.47	
ODI events/h	26.95 ± 13.78	
Medical History	**n (%)**	
Hypertension	47 (40.9%)	
Gastroesophageal reflux disease (GERD)	34 (29.6%)	
Depression	28 (24.3%)	

Hypercholesterolemia	25 (21.7%)
Hyperlipidemia	21 (18.3%)
Anxiety	21 (18.3%)

3.3. Study Objectives and Methods

The DREAM study was a multicenter, prospective, single-arm study. Patients were scheduled for screening and baseline evaluations before implant and follow-up post-surgery at 2, 3, 4, 5, 6, 8 and 10 months or 9 months, and a final follow-up at 12 months.

Effectiveness was evaluated by two co-primary endpoints:

- Percentage of responders at 12 months based on AHI4, a responder being defined as a participant who satisfies the following criteria: at least a 50% reduction from the average AHI4 of screening and baseline to 12 months post-surgery and a remaining AHI4 less than 20 at the 12-month visit (aka “Sher Criteria”).
- Percentage of responders at 12 months based on ODI4, a responder being defined as a participant who satisfies the following criterion: at least a 25% reduction from the average ODI4 of screening and baseline to 12 months post-surgery.

There were six secondary effectiveness endpoints, focusing on: OSA-specific quality of life measured by the SNORE-25 instrument; hypoxemic burden measured by the percentage of sleep time with oxyhemoglobin saturation< 90%; intermittent hypoxia measured by the ODI4; the sleep-specific function measured by the Functional Outcomes of Sleep Questionnaire (FOSQ-10); the sleep propensity measured by the Epworth Sleepiness Scale (ESS) and change in OSA severity.

Safety was evaluated by the incidence of device-related serious events (SAEs) recorded during the study for a period of 12 months post-surgery. Adverse events (AEs) were adjudicated by an independent Clinical Events Committee (CEC). An independent Data & Safety Monitoring Board (DSMB) reviewed the accumulated safety data and the validity and integrity of the data from the clinical study.

3.4. Safety Results

Out of the 115 patients in whom implant was attempted, 85 (73.9%) experienced a total of 252 non-serious device and/or implant procedure-related AEs (see Table 3 through Table 5). The non-serious procedure-related AEs observed were anticipated with this type of surgery including difficulty swallowing/dysphagia (11.7% of patients) and swelling at the incision site (12.2% of patients). Among the device-related non-serious events, 24.3% of patients experienced local skin irritation due to the Disposable Patch (DP), 14.8% of patients reported discomfort with the stimulation, and 12.2% experienced tongue discomfort. The same patient can experience various effects.

Table 3. Implant-Related Adverse Events

	Number of subjects	Percentage of subjects
Incision site swelling	14	12.2%

	Number of subjects	Percentage of subjects
Incision-related (hypoesthesia, hematoma, ingrown hair, paraesthesia, foreign body, pain, irritation, reaction, dermatitis, application site infection)	13	11.7%
Dysphagia	12	10.4%
Temporary tongue weakness (speech disorder, dysarthria, tongue movement disturbance)	10	9.0%
Post procedural pain (oropharyngeal pain, odynophagia, ear discomfort, glossodynia)	10	9.0%
Post surgical effects (fever, headache, anxiety, fatigue, discomfort, diarrhea, nausea)	9	8.1%
Anesthesia related (phlebitis, presyncope, dysphonia, cough, glossitis)	8	7.2%
Implant site hypoesthesia	7	6.1%
Procedural pain	7	6.1%
Post procedural contusion	6	5.2%
Miscellaneous (epistaxis, ageusia, jaw clicking, tinnitus)	5	4.5%
Post procedural swelling	3	2.6%
Implant site infection	1	0.9%
Tongue spasm	1	0.9%

Table 4. Device-Related Adverse Events

	Number of subjects	Percentage of subjects
Application site irritation	28	24.3%
Stimulation discomfort	17	14.8%
Glossodynia	14	12.2%
Tongue complications (discomfort, spasm, swollen, involuntary contractions, tongue abrasions, plicated tongue)	9	7.8%
Incision site-related (swelling, hemorrhage, site reaction)	8	7.0%
Other symptoms (dizziness, dyspepsia, gastroesophageal reflux, panic attack, tinnitus)	8	7.0%
Dysphagia	7	6.1%

	Number of subjects	Percentage of subjects
Pain (jaw, ear, oropharyngeal, neck)	6	5.2%
Application site reaction (rash)	5	4.3%
Medical device pain	4	3.5%
Glossitis	3	2.6%
Dysphonia	2	1.7%
Headache	2	1.7%
Somnolence, Sleep disorder	2	1.7%
Cough	1	0.9%
Hypoaesthesia oral	1	0.9%
Jaw disorder	1	0.9%
Application site ulcer	1	0.9%
Sensation of foreign body	1	0.9%

Table 5. Device and Implant - Related Adverse Events

	Number of subjects	Percentage of subjects
Dysphagia	2	1.7%
Back pain	1	0.9%
Cough	1	0.9%
Medical device pain	1	0.9%
Musculoskeletal discomfort	1	0.9%
Neck pain	1	0.9%
Oropharyngeal pain	1	0.9%
Pain in jaw	1	0.9%
Sleep disorder	1	0.9%
Somnolence	1	0.9%

Serious Adverse Events

Table 6 provides the summary of all SAEs through 12 months post-implantation.

Table 6: SAE Summary through 12 Months Post Implant – SAF Set (N=115)

Serious Events	m (n,%)
Unrelated to Genio® Device and Unrelated to Implant Procedure – Serious Adverse Events (SAE)	3 (2, 1.7%)
Genio® Device-Related and/or Implant Procedure-Related – Serious Adverse Events (SAE)	13 (13, 11.3%)*
• Genio® Device-Related	6 (6, 5.2%)*
• Genio® Implant Procedure-Related	6 (6, 5.2%)*
• Genio® Device and Implant Procedure-Related	1 (1, 0.9%)*

n: number of subjects with at least one event
% = (n row / N column x 100)
m: number of events
Note: A same subject can have more than one event
* The 13 serious adverse events include 1 case of repositioning surgery (procedure related) and 4 cases of replacement surgery (device-related) that were neither classified by the Study Investigators nor by the Clinical Events Committee (CEC) as serious adverse events. If these events are excluded from the list of SAEs, the overall incidence of device- and/or procedure-related SAEs up 12-months would be 7% (device-related: 1.7%, device- and procedure-related: 0.9%, procedure-related: 4.3%).

Table 7 provides the description of device and/or procedure related SAEs through 12 months post-implant to date.

Table 7. Serious Adverse Events 12 Months Post Implant – Safety Set (N=115)

Description of SAE	Detailed Event Description
Incision Site Hematoma	Two days post-implant surgery, patient had developed hematoma at the surgical incision site with increased neck swelling and worsening bruising of the neck requiring surgical evacuation of the hematoma. The event was resolved without sequelae 4 days later. Patient continued in the study through the 18-month visit.
Dysphagia	Patient reported inability to swallow while in the recovery room post-implant and was discharged 11 days later in stable condition. The patient exited the study 10 days after discharge with the event ongoing and opted to keep the device implanted.
Dysphagia	Patient experienced impaired swallowing on the day of implant surgery. Hospital stay was extended due to trouble related to speech and swallowing from poor tongue motion. Edema was noted at the floor of the mouth edema. The event was fully resolved without sequelae a month later and assessed. Patient remains active in the study through the M36 visit.

Description of SAE	Detailed Event Description
Epistaxis	Patient experienced epistaxis on the right side 5 days post-implant surgery and was admitted to the emergency room with intermittent nasal bleeding from abrasions secondary to attempted nasal intubation during the implant surgery. The patient was discharged 2 days later; however, intermittent nasal bleeding persisted for approximately 50 days after discharge. Event was fully resolved without sequelae. The patient remained in the study until the M24 visit and was exited 4 months after with the device kept implanted.
Bundle Branch Block Left	Patient developed ventricular ectopy and new left bundle branch block at the end of the implant surgery procedure. The patient was admitted for cardiac monitoring and discharged the next day with the event fully resolved without sequalae. Patient remained active in the study through the M18 visit and was exited from the study 2 months later due to lost to follow-up with the device kept implanted.
Device Dislocation (Explant Surgery at 8 months)	Patient experienced a lack of stimulation approximately 253 days post implant surgery. A revision surgery was performed and the Implantable Stimulator (IS) was found to have migrated to one side. Due to the tight space between the hyoid bone and mandible, replacement or revision was not possible and the device was explanted without further complications. Patient exited the study a few months later.
Device Extrusion (Explant Surgery at 10 months)	Patient reported the Implantable Stimulator (IS) was protruding through the back of the gum approximately 310 days post implant surgery. Two months prior to this event, patient underwent a planned dental implant procedure to the floor of the mouth which was followed by a significant change in the stimulation amplitude. The IS was surgically removed about 2 weeks later without complications. Patient exited the study 3 weeks post explant surgery.
Device Dislocation (Explant Surgery at 2 months)	Patient reported increased swelling under the chin without pain, approximately 2 months post-implant surgery and reported no sensation or physical response to stimulation. X-ray showed disoriented and migrated device. Patient underwent explant surgery a month later without complications. Patient exited the study 2 weeks post-surgery.
Replacement Surgery at 6 Months *	Patient experienced inconsistent stimulation with suspected retrusor branch of the HGN included during implant as the Investigator did not observe straight tongue protrusion. During surgical intervention no migration was identified but excessive scarring was noted, preventing replacement. Device was explanted without complications.
Replacement Surgery at 6 Months *	Patient reported stimulation discomfort and intermittent stimulation. External component troubleshooting revealed atypical device activity. During surgical intervention it was confirmed the device had not migrated. The device was successfully replaced without complication with consistent stimulation observed from new device during intra-operative testing. Patient continued in the study.

Description of SAE	Detailed Event Description
Replacement Surgery at 11 Months *	Patient experienced inconsistent stimulation that could not be resolved with external component troubleshooting. During surgical intervention the device was tested with no response. Device was successfully removed and replaced with consistent stimulation observed from new device during intra-operative testing. Patient continued in the study.
Replacement Surgery at 12 Months *	Patient experienced loss of stimulation that could not be resolved with external component troubleshooting. Migration noted in X-ray with migration of right paddle confirmed during intervention. Excessive scarring prevented replacement and device was explanted without complications.
Repositioning Surgery at 9 Months *	Patient had mixed hypoglossal nerve activation on the left noted when the device was activated. The Investigator repositioned the device to exclude retrusor branches from receiving stimulation.

* The 1 case of repositioning surgery and 4 cases of replacement surgery were neither classified by the Study Investigators nor adjudicated by the Clinical Events Committee (CEC) as serious adverse events.

Post-Month 12 Safety Data

A subset of active study subjects have completed 24-month and 36-month timepoints as shown in Table 8 below.

Table 8. Summary of Study Subjects with Post M12 Study Timepoints

Months	Subjects
24-Month	74
36-Month	30
48-Month	0

A summary of safety events post-Month 12 has been provided in the Table 9 below.

Table 9. Adverse Event Summary Post-Month 12 up to April 30, 2025

Adverse events	Non-device-related Non-procedure-related m (n, %)	Device or Procedure-related m (n, %)
Non-serious	97 (46, 40.0%) (AE)	29 (22, 19.1%) (AE)
Serious	11 (5, 4.3%) (SAE)	5 (5, 4.3%) (SAE)

n: number of subjects with at least one event
% = (n row / N column x 100)
m: number of events

Note: A same subject can have more than one event

* The 5 serious adverse events include 2 cases of replacement surgery and 3 cases of explant surgery that were neither classified by Study Investigators nor adjudicated by the Clinical Events Committee (CEC) as serious adverse events.

Table 10 below presents a summary of all serious adverse events related to surgical interventions experienced by subjects in the DREAM study presented by month of intervention (up to April 30, 2025).

Table 10. Serious Adverse Events Related to Surgical Interventions Post-Month 12 *

Post-Surgical Intervention	Reason for Surgical Intervention	Surgical Intervention / Complications	Surgical Outcome	Subject Disposition
Explant Surgery at 17 Months	Device Deficiency: Subject feeling inconsistent stimulation. Unable to resolve with external component troubleshooting. Investigator and patient decided to explant device.	During the intervention, it was confirmed that the device had not migrated. Device tested and no stimulation observed. Device explanted without complication.	The device was successfully explanted.	No adverse events observed or reported post-operatively.
Explant Surgery at 22 Months	Device Deficiency: No stimulation felt. Unable to be resolved through external component troubleshooting. Decision was made to explant.	The device was explanted without complication.	The device was successfully explanted.	No adverse events observed or reported post-operatively.
Explant Surgery at 28 Months	Device Deficiency: Inconsistent connectivity of device. External component troubleshooting did not resolve the issue which led to deeming it to be IS related. The subject elected to have the device explanted.	During the intervention, calcification was noted on the body of the device. The device was removed without complication.	The device was successfully explanted.	No adverse events observed or reported post-operatively.
Replacement Surgery at 16 Months	Device Deficiency: Potential migration of the device after MVA. Following the incident, subject experienced inconsistent stimulation.	Migration confirmed during intervention. Scaring and encapsulation were present, device	Consistent stimulation observed from new device during intra	Subject continued in the study. No adverse events observed or reported post-operatively.

	Unable to resolve with external component troubleshooting.	replaced successfully with no complications.	operative testing.	
Replacement Surgery at 21 Months	Device Deficiency: Subject feeling inconsistent stimulation. Unable to resolve with external component troubleshooting.	The device was successfully replaced without complications.	Consistent stimulation observed from new device during intra – operative testing.	No adverse events observed or reported post-operatively.

* The 5 serious adverse events include 2 cases of replacement surgery and 3 cases of explant surgery that were neither classified by the Study Investigators nor adjudicated by the Clinical Events Committee (CEC) as serious adverse events.

3.5. Efficacy Results

The efficacy of OSA symptom reduction was evaluated through two main parameters: the apnea hypopnea index (AHI) and the oxygen desaturation index (ODI). All the sleep studies were scored by an independent core laboratory, and the patient was required to sleep a minimum of 4h, with at least 1h being in the supine position.

At the 12-month post-implant PSG, the AHI responder rate was 63.5% (73/115), and the ODI responder rate was 71.3% (82/115) with a median reduction of 70.8% in AHI and 72.1% in ODI (Table 11). The improvement occurred in all sleeping positions, which reflected in the non-supine and supine AHI of 12.7±12.8 events/hr and 48.9±19.6 events/hr, respectively (n=110) being reduced to 5.2±8.2 events/hr and 22.7±19.9 events/hr (n=89, p<0.001). In summary, overall median AHI reduction (70.8%), median reduction in supine (66.6%) and median AHI reduction in non-supine (71.0%) sleep positions were comparable.

Table 11. Effectiveness Results

Primary Endpoint	Responder Rate	*p* value
AHI Response Rate M12	63.5% (73/115)	0.002
ODI Response Rate M12	71.3% (82/115)	< 0.001

Additionally, OSA symptoms and quality of life were assessed with questionnaires: 10-item Functional Outcomes of Sleep Questionnaire (FOSQ-10) and the Epworth Sleepiness Scale (ESS) questionnaire. The average scores at 12 months showed clinically relevant improvement in both symptoms and quality of life (see Table 12).

Table 12. Secondary Effectiveness Endpoints

	Baseline (N=110) Mean ± standard deviation	Month 12 (N=89) Mean ± standard deviation
SNORE-25 total score	1.61 ± 0.88	0.59 ± 0.62
Total sleep time SaO2 < 90% (min)	45.18 ± 45.83	18.02 ± 30.34
Oxygen Desaturation Index (ODI) (events/hour)	26.95 ± 13.78	9.15 ± 9.60
FOSQ-10 total score	15.92 ± 2.94	18.19 ± 1.94
ESS total score	9.64 ± 5.56	6.22 ± 4.12
Apnea-Hypopnea Index (AHI) (events/hour)	28.00 ± 11.47	9.52 ± 9.43

Subgroup analyses for gender, age, race, and BMI segmented by OSA severity were performed and can be found in Table 13. In all subgroup analyses, except for the one based on race, there was a significant overlap in the confidence intervals of the various groups. This overlap confirms that there are no significant differences in treatment responses among the different subgroups.

Table 13. Percentage of AHI and ODI at Month 12 for the various subgroups

Subgroups		Percentage of Responders at Month 12 – Full Analysis Set (N=110) Worst Case Imputation			
		n	n (%) of imputed missing values	Rate (n /N) of participants with 50% Reduction in AHI from baseline and AHI < 20 [95% CI]	Rate (n /N) of participants with 25% Reduction in ODI from baseline [95% CI]
Gender	**Male (N=78)**	78	16 (20.5%)	62.8% (49/78) [51.1% ; 73.5%]	71.8% (56/78) [60.5% ; 81.4%]
	Female (N=32)	32	5 (15.6%)	75.0% (24/32) [56.6% ; 88.5%]	81.3% (26/32) [63.6% ; 92.8%]
Age	**Age<52 (N=26)**	26	8 (30.8%)	53.8% (14/26) [33.4% ; 73.4%]	65.4% (17/26) [44.3% ; 82.8%]
	52≤Age≤62 (N=58)	58	10 (17.2%)	72.4% (42/58) [59.1% ; 83.3%]	79.3% (46/58) [66.6% ; 88.8%]
Race	**White (N=104)**	104	21 (20.2%)	64.4% (67/104) [54.4% ; 73.6%]	73.1% (76/104) [63.5% ; 81.3%]
	Black or African American (N=4)	4	0 (0.0%)	100.0% (4/4) [39.8% ; 100.0%]	100.0% (4/4) [39.8% ; 100.0%]
	Other (N=2)	2	0 (0.0%)	100.0% (2/2) [15.8% ; 100.0%]	100.0% (2/2) [15.8% ; 100.0%]

Subgroups		Percentage of Responders at Month 12 – Full Analysis Set (N=110) Worst Case Imputation			
		n	n (%) of imputed missing values	Rate (n /N) of participants with 50% Reduction in AHI from baseline and AHI < 20 [95% CI]	Rate (n /N) of participants with 25% Reduction in ODI from baseline [95% CI]
BMI	**BMI≤25 (N=15)**	15	4 (26.7%)	66.7% (10/15) [38.4% ; 88.2%]	66.7% (10/15) [38.4% ; 88.2%]
	25<BMI≤28 (N=34)	34	5 (14.7%)	73.5% (25/34) [55.6% ; 87.1%]	85.3% (29/34) [68.9% ; 95.0%]
	28<BMI≤30 (N=27)	27	5 (18.5%)	59.3% (16/27) [38.8% ; 77.6%]	70.4% (19/27) [49.8% ; 86.2%]
	30<BMI≤32 (N=30)	30	7 (23.3%)	63.3% (19/30) [43.9% ; 80.1%]	70.0% (21/30) [50.6% ; 85.3%]
	BMI>32 (N=4)	4	0 (0.0%)	75.0% (3/4) [19.4% ; 99.4%]	75.0% (3/4) [19.4% ; 99.4%]

3.6. Conclusion

The DREAM study results supported FDA approval of the Genio® device for the treatment of adults with moderate to severe OSA, in both supine and non-supine sleep positions, who have not tolerated, failed or refused PAP therapy. If you would like more information, please contact your healthcare provider.

3.7. Safety and Effectiveness Data from OUS Post-market Clinical Follow-up Study (EliSA)

Upon CE Mark approval of the Genio® System, Nyxoah initiated the EliSA trial, a post market clinical follow up (PMCF) study. The purpose of this study is to assess the long-term safety and performance of the Genio® System and to identify any potential new risks not previously encountered during the pivotal study. Data was collected under normal conditions of use.

The EliSA study includes collection of performance related data (e.g., change of AHI, change of ODI, etc.) as well as safety data (collection of adverse events and device deficiencies). The primary and secondary outcomes for the EliSA study differ from those used for the DREAM study (i.e., change in AHI vs. responder rates). Additionally, the inclusion and exclusion criteria in EliSA allows for the enrollment of patients more severe OSA symptoms (higher mean AHI with fewer restrictions on co-morbidities or exclusionary medications) and those with a higher BMI level than what was allowed in the DREAM study.

The EliSA study aims to include 110 implanted patients with a 5-year follow-up period. As of December 12th, 2024, 101 patients have been implanted in Germany, the Netherlands, Belgium and Switzerland. The enrollment is still ongoing, and currently, only 57.3% (n=63) of the subjects have completed the month 12 follow-up. A total of six (6) SADEs and 184 ADEs (183 confirmed by the CEC) have been reported[1].

[1] Note that the CEC adjudication is ongoing and hence the AE classification is subject to modification

The preliminary results from the EliSA study are provided in Table 14 below. The responder rate based on Sher criteria (Table 15) and the line plot showing baseline and final AHI (Figure 1 below) are also provided.

Table 14. EliSA preliminary AHI and ODI results for subjects completing month 12 follow-up

EliSA preliminary results	Screening (Mean±SD)	M12 (Mean±SD)	Mean change (Mean±SD)	% change (Mean±SD)
AHI (N=63)	36.1±14.2	24.7±17.1	-11.4±15.8	-30.5±40.1
ODI (N=62)	31.8±15.2	25.5±17.1	-6.3±15.9	-16.0±50.5

Table 15. EliSA preliminary responder rates for subjects completing month 12 follow-up

Responder Rates	
AHI Responder	41.3%
AHI Sher Responder	38.1%
ODI Responder	51.6%
AHI responder = 50% improvement from screening AHI Sher responder = 50% improvement + residual AHI < 20 ODI responder = 25% improvement from screening	

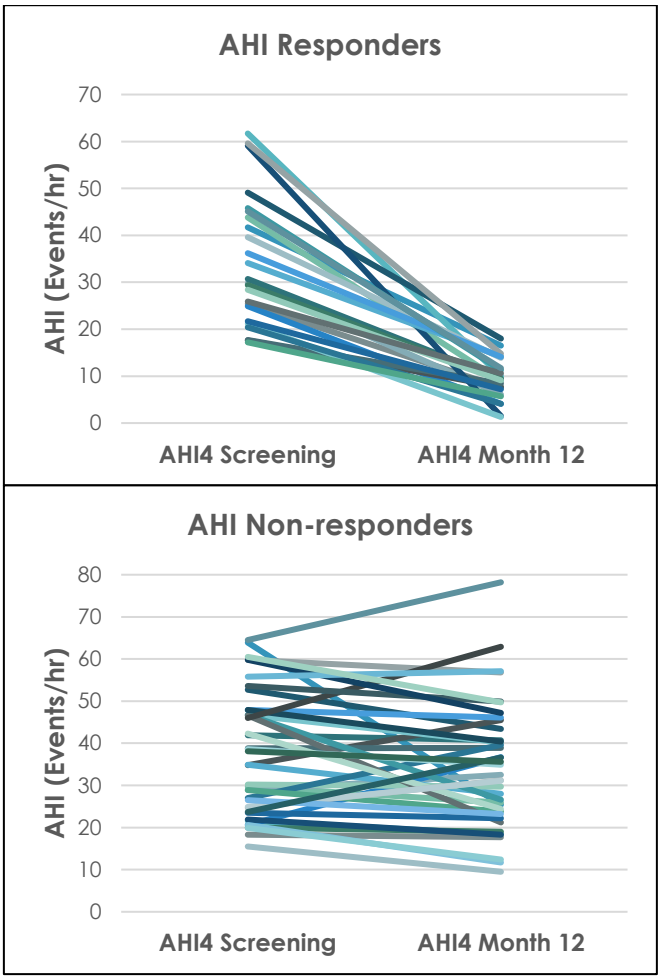


Figure 1. Line plot showing preliminary data for baseline and final AHI for EliSA study subjects (responders and non-responders) completing month 12 follow-up

As described previously, the data presented for the EliSA study is preliminary as there was no planned interim analysis defined apriori in the study protocol. The study was conducted in a real-world setup where patients were afforded fewer (just one mandatory PSG) opportunities to be titrated to optimal therapy response through a full night PSG prior to their 12-month visit. Moreover, the titration algorithm of Genio® therapy has been refined since these patients were implanted as witnessed by the improvement in responder rate in the DREAM study.

4. Your Genio® System

4.1. Therapy Overview

The Genio® System 2.1 consists of one implanted device, the Implantable Stimulator, and three external devices: the Activation Chip, the Disposable Patch and the Charging Unit.

The Implantable Stimulator will be implanted under your chin during a short surgical procedure. After a healing period of approximately eight (8) weeks, you will receive a Patient Kit containing your external devices, and your implant will be activated for the first time. In order to find an optimal therapy program for you, an adjustment phase is required and can take several months. During this optimization period, you will have clinic visits and overnight sleep studies. Your health care provider will determine when sleep studies are needed. Adjusting your device for optimal effects is normal and may require multiple visits with your health care provider.

To achieve good results, it is very important to follow your visit schedule and to use the system every night.

4.2. Patient Kit Contents

The enclosed Patient Kit contains the following components:

- An Activation Chip in a protective cover
- A Charging Unit with country specific power adapters (EU, US, AUS and UK)
- Disposable Patches
- This Patient Manual
- A Quick Setup Guide

4.3. The Genio® System 2.1 Components

The Genio® System 2.1 includes the following components: the Implantable Stimulator, the Activation Chip, the Disposable Patch and the Charging Unit.

4.3.1. Implantable Stimulator

The Implantable Stimulator is a small saddle-shaped implant (about 25 mm x 20 mm x 20 mm – L x W x H) that consists of an antenna (“the saddle” or “flat part”) and two “legs” with two metal pads each, called electrodes. This implant is surgically implanted under the chin during a surgical procedure close to a nerve of the tongue, called the hypoglossal nerve. The electrodes allow stimulation energy to flow to the hypoglossal nerve, resulting in the stimulation of the nerve and contraction of the tongue muscles. This process can help maintain open airway and normalize breathing while sleeping.

4.3.2. Activation Chip

The Activation Chip is the power source of the Implantable Stimulator. It contains a rechargeable battery and is programmed with therapy settings as determined by your health care provider. The Activation Chip should be kept in the provided protective cover when it is not in use or not being charged. You will be required to charge the Activation Chip daily.

4.3.3. Charging Unit

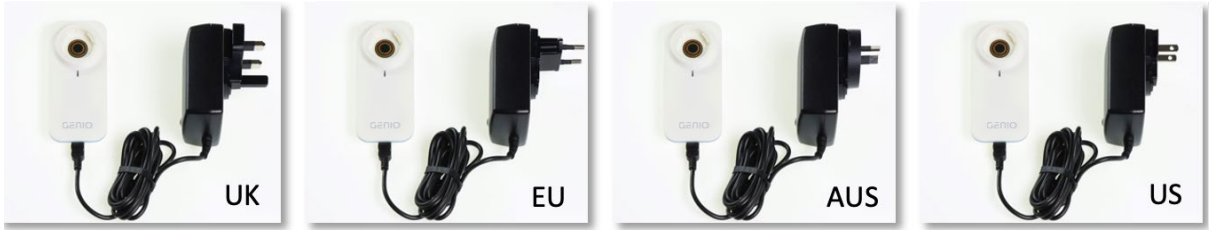
The Charging Unit and its power adapter are used to charge the Activation Chip's battery during the day, in order to be ready for the next night. The Activation Chip can take up to three hours to fully charge. The Charging Unit uses a power adapter supplied by Nyxoah with four country specific sockets (EU, US, AUS and UK) and provides 100-240 V/50-60Hz.

4.3.4. Disposable Patch

The Disposable Patch is a single-use adhesive patch that is placed on the skin under the chin. When the Activation Chip is snapped into the Disposable Patch's clip, they work together to transmit stimulation energy to the Implantable Stimulator. The Disposable Patch should not be used after its expiration date.

4.4. Preparing Your Genio® System 2.1 for Use

Step 1 - Connect the power adapter cable's micro-USB to the Charging Unit. The country specific connectors are easy to attach to your power adapter. Having the different connectors will make it easier for you to travel to countries other than your home country and utilize your Genio® System 2.1.



Step 2 -

Plug the power adapter into an electrical outlet and place the Charging Unit on a firm surface and, if possible, close to your bed to make nightly resets easier if necessary.

The green lights on the power adapter and Charging Unit turn on to indicate proper connection to the power outlet.

CAUTION: Use **only** the power adapters provided by Nyxoah. Use of other adapters may damage the device.

Step 3 - **Carefully** remove the Activation Chip from its protective cover by gently pushing down one of the three tabs with one hand and pulling out the Activation Chip with the other hand.

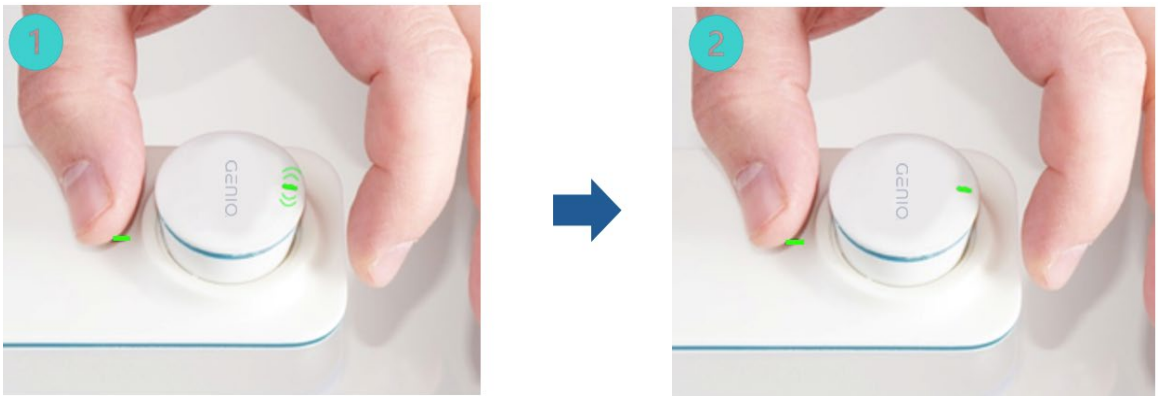
CAUTION: Do NOT touch the metal pins on the bottom of the Activation Chip and do NOT place these metal pins on any surface as they can be damaged.

Step 4 - Place the Activation Chip in the docking area of the Charging Unit to charge it.

CAUTION: Do NOT use excessive force when inserting Activation Chip to the Charging Unit or when removing it.

(1) If the Activation Chip is not fully charged when placed in the Charging Unit, a blinking green light displays on the Activation Chip, indicating charging.

(2) Once the charging process is complete and the Activation Chip is fully charged, the Activation Chip displays a steady green light.



Blinking green light: Charging in process

Steady green light: Charging complete

Note: A summary of the light indications of the device is available in Section 8 "Visual Indications".

You are all set! Start using your Genio® System 2.1 and enjoy restful nights!

5. Using Your Genio® System

5.1.1. Good evening! Have a restful night

Follow these steps prior to going to sleep:

Step 1 - Place a **new** Disposable Patch on a firm surface with the removable liners facing the surface and the plastic clip facing upwards.

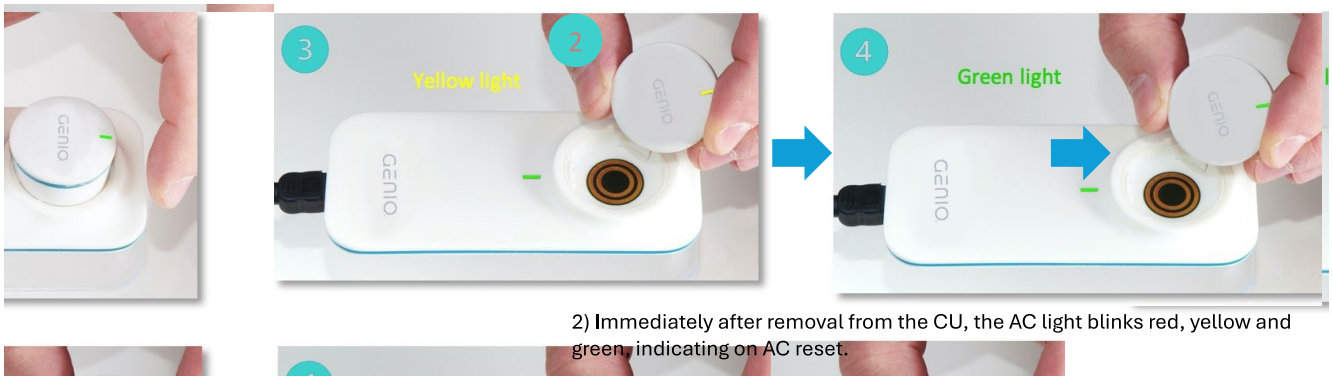
> **CAUTION:** Do NOT re-use Disposable Patches. Re-using the Disposable Patch may lead to lack of adherence to the skin resulting in potential loss of therapy.
> Disposable Patches should not be used after the expiration date marked on the package.

> **CAUTION:** Do NOT place the Disposable Patch on a metallic surface or near any type of metal. Attempting to attach the Activation Chip while the Disposable Patch is close to a metal may cause device malfunction.

Step 2 - Verify that the Activation Chip displays a solid green light, which means that it is fully charged. Gently remove the fully charged Activation Chip from the Charging Unit. This resets the Activation Chip.

CAUTION: Do NOT touch the metal pins on the bottom of the Activation Chip and do NOT place these metal pins on any surface as they can be damaged.

When removed from the Charging Unit, the Activation Chip light blinks red, yellow and green once, indicating that it has been reset and is ready to be used.



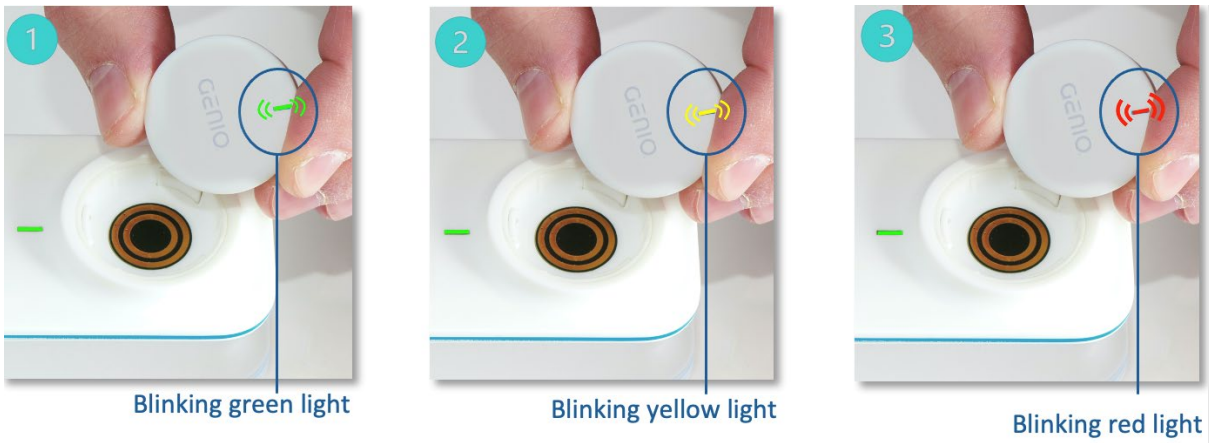
2) Immediately after removal from the CU, the AC light blinks red, yellow and green, indicating on AC reset.

Step 3 - Once the Activation Chip has been reset, it blinks until a Disposable Patch is connected:

(1) If the blinking light on the Activation Chip is green, it means the Activation Chip is charged and ready to be connected to a Disposable Patch.

(2) If the blinking light on the Activation Chip is yellow, it means the Activation Chip battery is low and may not last for an entire night. If possible, return the Activation Chip to the Charging Unit until the battery is fully charged.

(3) If the blinking light on the Activation Chip is red, it means the Activation Chip is malfunctioning. The Genio® System 2.1 cannot be used until the chip is replaced. If this occurs, contact your health care provider as soon as possible for a new Activation Chip.



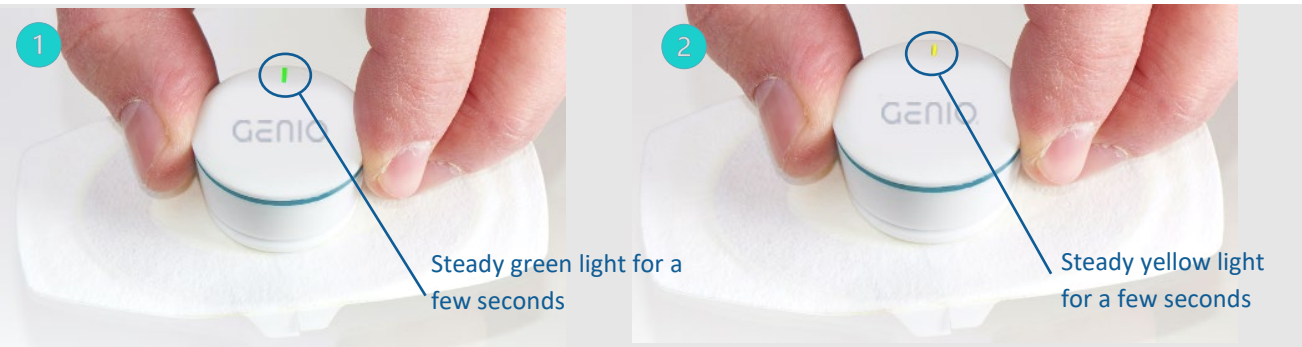
Step 4 - With the Activation Chip light still blinking green, connect the Activation Chip firmly to the clip on the Disposable Patch (you should hear a clicking sound). It should attach to the Disposable Patch with very little effort.

If the Activation Chip light stops blinking before you make the connection, return the Activation Chip to the Charging Unit to reset it, and return to Step 2.

If connection is successful, the Activation Chip light shows a steady light for a few seconds only:

(1) If the steady light on the Activation Chip is green (for a few seconds only), it means the Activation Chip battery is charged and ready for a full night of use.

(2) If the steady light on the Activation Chip is yellow (for a few seconds only, it means the Activation Chip battery is low and may not last for an entire night of use.



Note: A summary of the light indications of the devices is available in Section 8 "Visual Indications".

CAUTION: Do NOT use excessive force when connecting the Activation Chip to the Disposable Patch.

Step 5 - Peel off the two adhesive liners from the bottom of the Disposable Patch.

CAUTION: For male users – Before placing the Disposable Patch, make sure to carefully shave the area under your chin. The Disposable Patch works best on skin that has been shaved within the last 17 hours.

CAUTION: Before applying the Disposable Patch, carefully wash off all facial creams on the skin under your chin. Residual cream on this area may prevent the Disposable Patch from staying attached.

CAUTION: Do NOT fold the Disposable Patch while removing the adhesive liners.

CAUTION: Do NOT apply the Disposable Patch on breached or wounded skin (such as scrapes, cuts, burns, rashes, breakouts, etc.) as this could damage the skin

Step 6 - Tilt your head back. Using a mirror, apply only the center of the Disposable Patch with the attached Activation Chip under your chin as illustrated on the picture below. The incision scar can be used as a reference point for optimal placement. Align the Activation Chip in the middle of your chin.

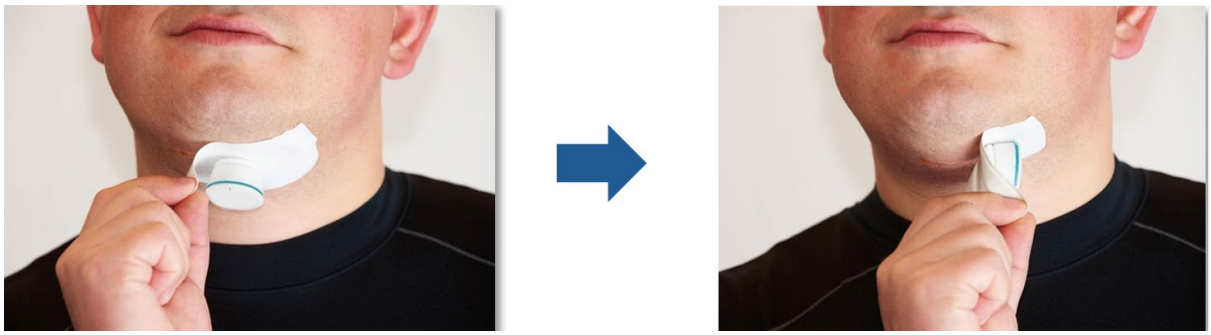
Step 7 - Return your head to a normal position. Beginning from the center and moving to the edges, flatten the edges of the Disposable Patch with your fingers to ensure proper patch adhesion.

The system is now activated. You can go to sleep and enjoy a restful night. The stimulation will start automatically after the delay time set by your health care provider. The delay time is a period during which no stimulation is delivered in order to allow you to fall asleep without feeling the stimulation.

5.1.2. Good morning! Have a wonderful day

Once you get up, follow these steps:

Step 1 - Remove the Disposable Patch with the attached Activation Chip from your skin. The removal shall be done from left to right or right to left and as close as possible to the skin to minimize potential skin irritation. If you experience skin irritation where the patch was attached, consult your health care provider.



Step 2 - Disconnect the Activation Chip from the Disposable Patch.

CAUTION: Do NOT touch the metal pins on the bottom of the Activation Chip and do NOT place these metal pins on any surface as they can be damaged.

Step 3 - Discard the Disposable Patch.

Note: It is recommended that all used Disposable Patches be brought to an electronic waste recycler as they contain printed circuit boards which should not be landfilled.

Step 4 - Place the Activation Chip in the Charging Unit to charge it so that it will be ready for the next night.

CAUTION: The Activation Chip must be fully charged after each use.

Verify that the green light on the Charging Unit is on, indicating it is properly connected to power.

Verify that the green light on the Activation Chip starts blinking, indicating that the Activation Chip battery is charging. Charging may take up to three hours.

Note: If the green light of the Activation Chip remains constantly on, it means that the battery of the Activation Chip is still fully charged because your therapy settings do not require a lot of energy.

CAUTION: The Activation Chip must be fully charged after each use.

CAUTION: If the light does not turn on the Activation Chip, it may mean that the Charging Unit is not properly connected to power. Verify the connection (1) between the adapter and the electrical outlet (green light on power adapter), (2) between the Charging Unit and the adapter (green light on the Charging Unit) and (3) between the Activation Chip and the Charging Unit (green light on Activation chip).

Note: A summary of the light indications of the devices is available in Section 8 "Visual Indications."

6. Genio® Smartphone Application

The Genio® Smartphone Application communicates with your Activation Chip and allows you to perform the following actions:

- Pause and resume treatment
- Adjust stimulation intensity within a pre-defined safe range
- Access usage information

6.1. Installation and Setup

Before you can use your Genio® Smartphone Application, Nyxoah field personnel will help you to:

- Install the Genio® Smartphone Application on your phone (iPhone or Android)

- Setup your Genio® Smartphone Application and configure it to your geographical region
- Pair your Activation Chip with the Genio® Smartphone Application so you can begin using the features of the App

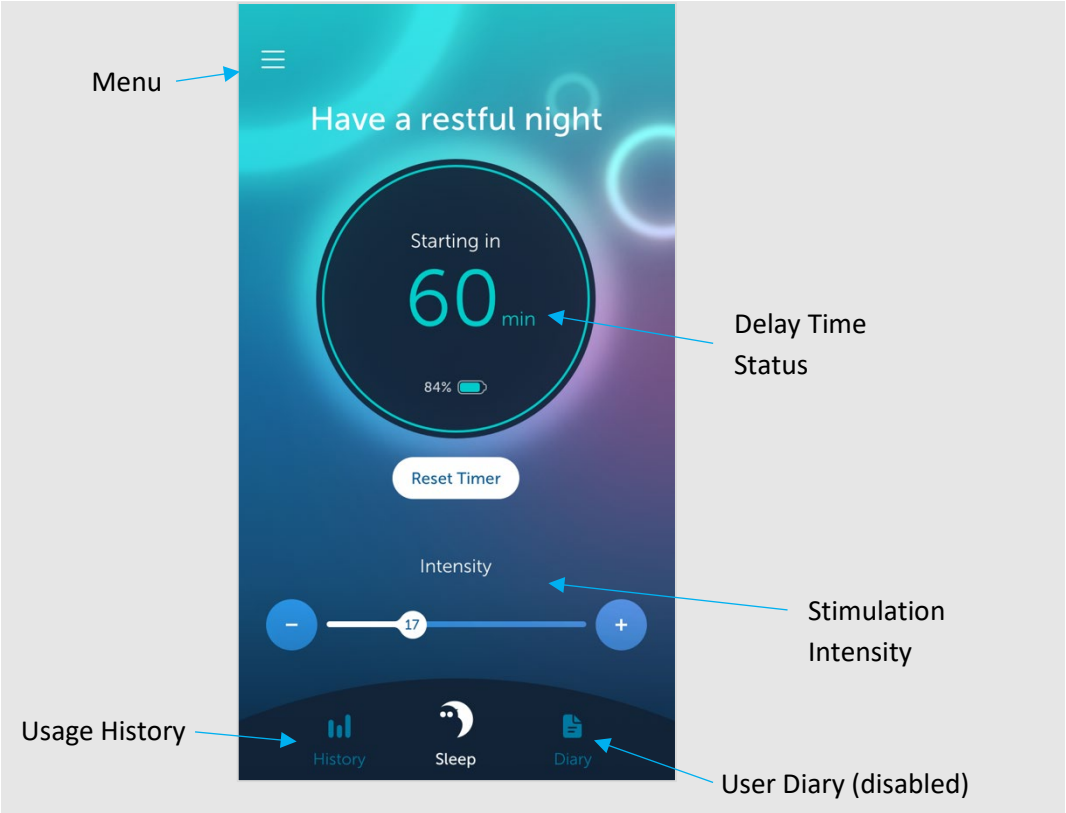
Typically, Nyxoah field personnel will perform these steps for you as part of your initial activation visit. If after your activation visit you need assistance with any of the installation, setup or pairing actions associated with the Genio® Smartphone Application, please contact Nyxoah.

6.2. Daily Use

On a daily basis, the Genio® Smartphone Application allows you to (see picture below):

1. Control your Genio® therapy. You can pause/ or resume stimulation, adjust the stimulation intensity, and reset the delay time to its pre-set value.
2. Access usage history data.

These features are detailed in the following sections.

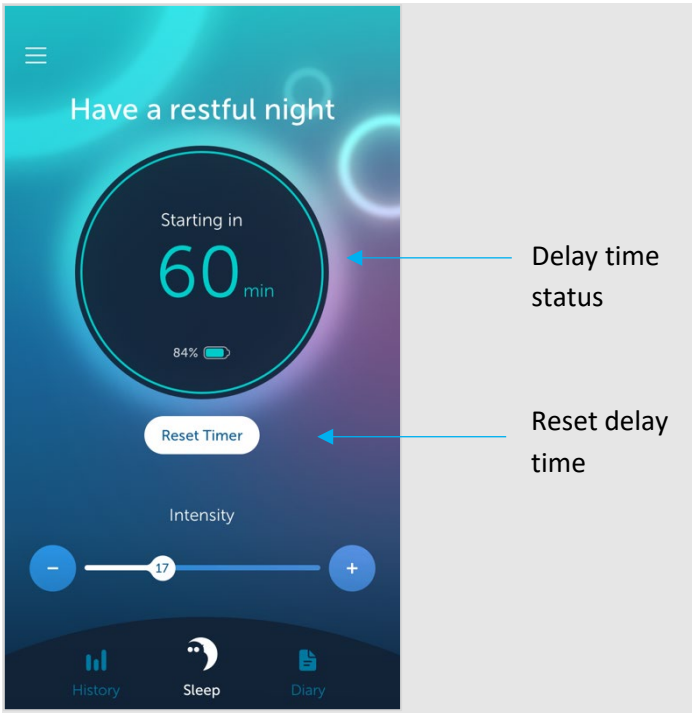


6.2.1. Control your Genio® Therapy

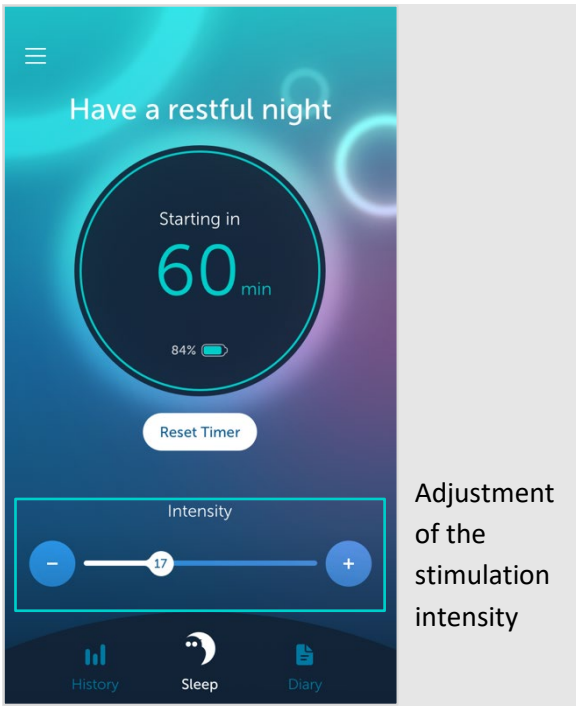
Once your Genio® System 2.1 is properly setup according to Section 4, "Your Genio® System," the Genio® Smartphone Application allows you to control your therapy on three different levels:

1. **Delay time:** As soon as the Disposable Patch is connected to the Activation Chip, the countdown of your predefined delay time starts, after which the stimulation will be

activated. The remaining time will be displayed on your Genio® Smartphone App. If you need more time and want to reset your delay time, press on “Reset timer”.



2. **Stimulation intensity adjustment:** When the Activation Chip is connected to a patch and communicates with it, the application can be used to adjust the intensity of the stimulation within a range defined by your sleep physician by pressing the + or – buttons.

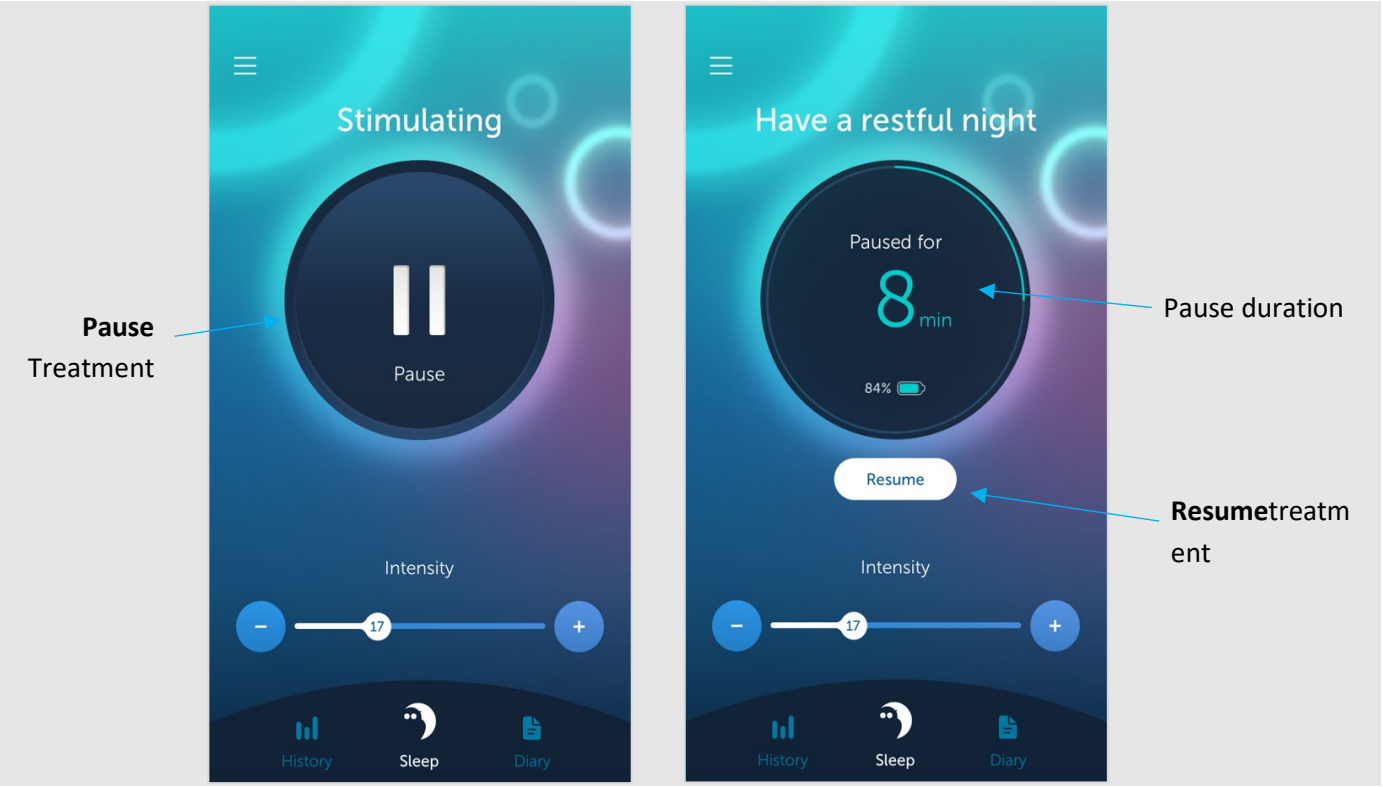


Adjusting the stimulation intensity can be done at any time:

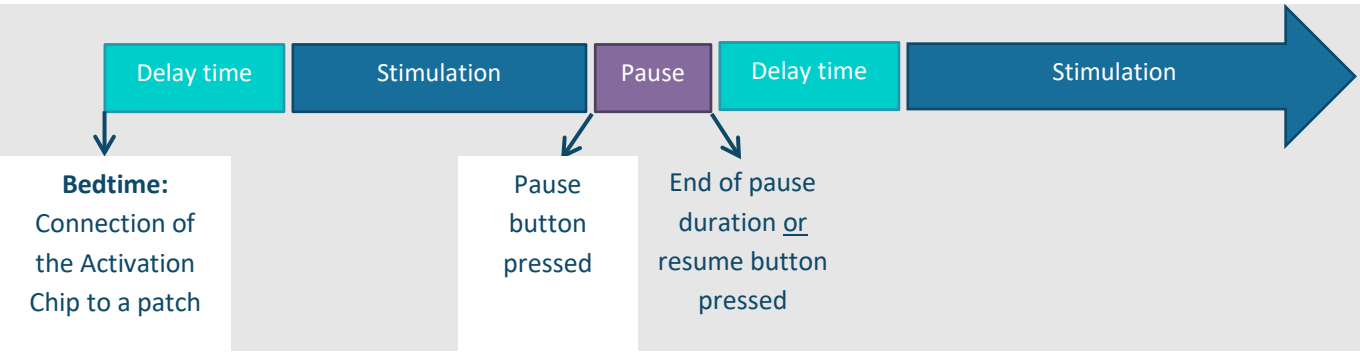
- If the intensity is modified during the delay time, a single stimulation pulse will be felt, allowing you to assess if the newly set intensity is suitable for you. Wait until the end of this pulse before further changing the intensity.
- If the intensity is changed while the stimulation is on, the change in intensity will be implemented for the next stimulation period (typically a few seconds later).

When updating the stimulation intensity, the selected intensity will be updated on the screen and the delay timer will reset.

3. **Pause/Resume:** At the end of the delay time, the stimulation starts. You can **pause** stimulation for a predefined duration by pressing the "Pause" button (see picture below, on the left). Once treatment is paused, a pause timer will be displayed (see picture below, on the right), based on the pause duration defined in the Smartphone Application settings (see "Settings" section below).



To **resume** treatment, you can either press "Resume" (see picture above, on the right) or wait until the end of the pause duration. In both cases, the stimulation will start again at the end of your predefined delay time.



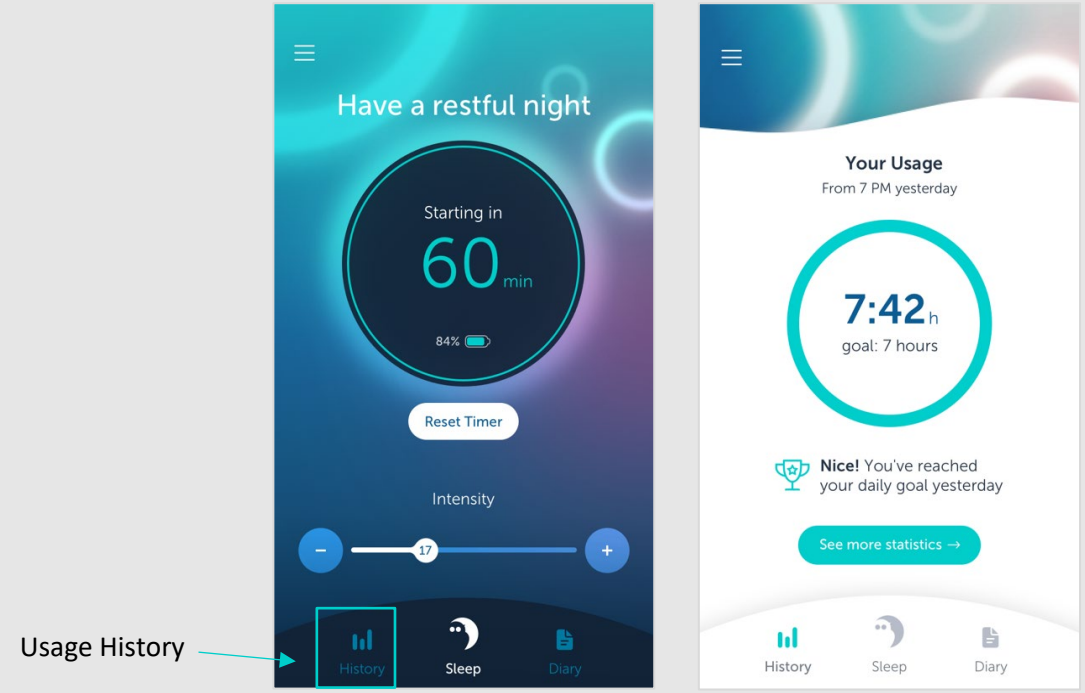
Note: in case of a wireless communication interference between the Smartphone Application and your Activation Chip, make sure your Activation Chip is not located near large metallic surfaces or other Bluetooth devices and retry using the Smartphone Application. See Section 7.5.5 for additional troubleshooting information.

6.2.2. History Screen

The Genio® Smartphone Application provides information regarding the daily usage of your Genio® System 2.1.

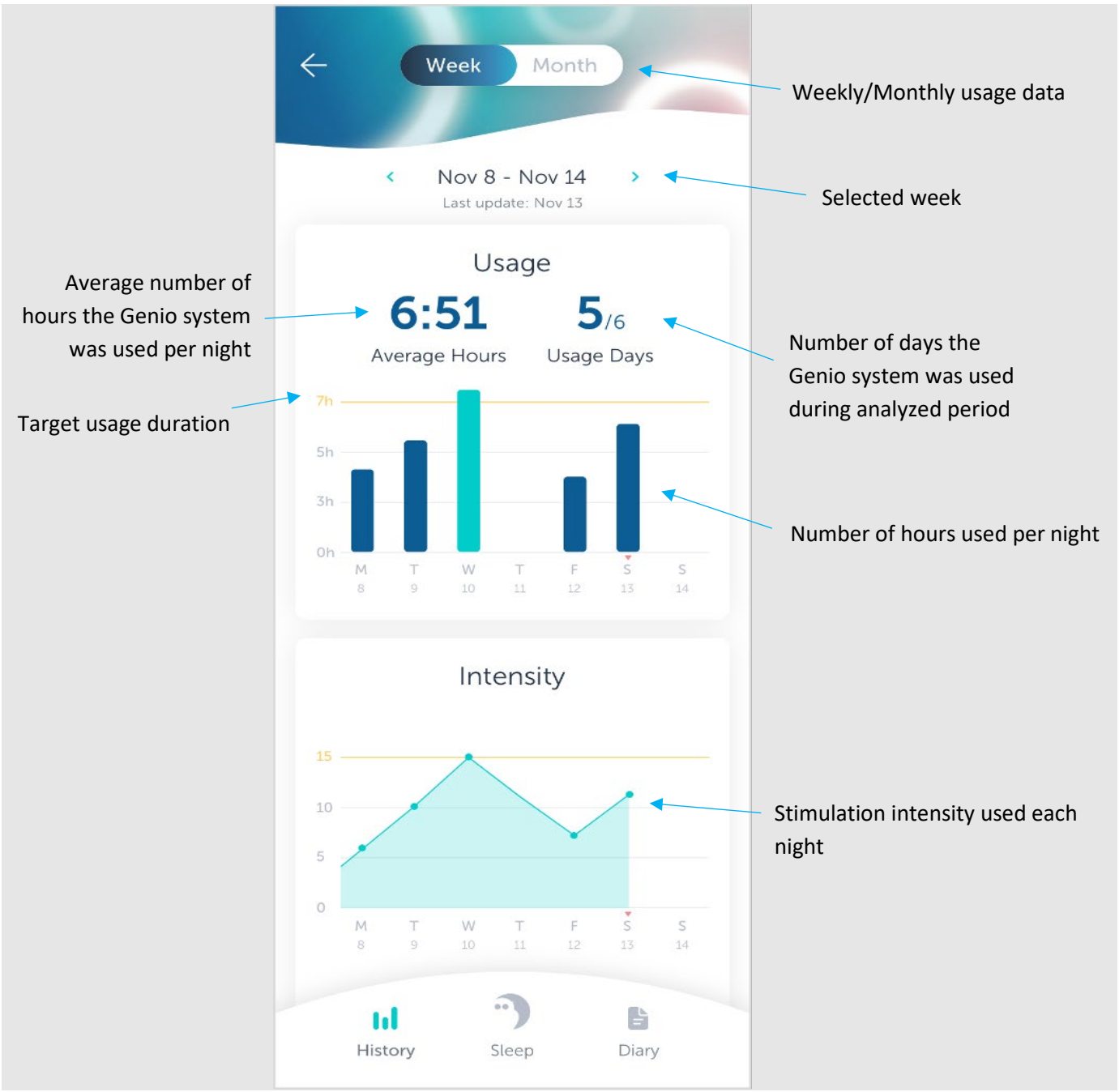
To view your usage data, ensure your Activation Chip is connected to a Disposable Patch and in proximity of your smartphone and press the "History" button (see right picture below). The Smartphone Application will display your usage data of the previous night retrieved from the Activation Chip (see left picture below). To view more detailed statistics regarding your weekly or monthly use of the Genio® System 2.1, press the "See more statistics" button.

Note: The Activation Chip stores last night's log record only after it has been reset by placing in the Charging Unit. For the history view to include the last use period, make sure that the Activation Chip is reset before it is reconnected to a Disposable Patch and to the Smartphone Application.
Note: The History screen is not available during stimulation. If your Activation Chip is stimulating, pause the treatment to access the History screen.
Note: When entering the History screen for the first time since the Smartphone Application was launched, if the Activation Chip is in the Delay period, the Delay timer will reset.



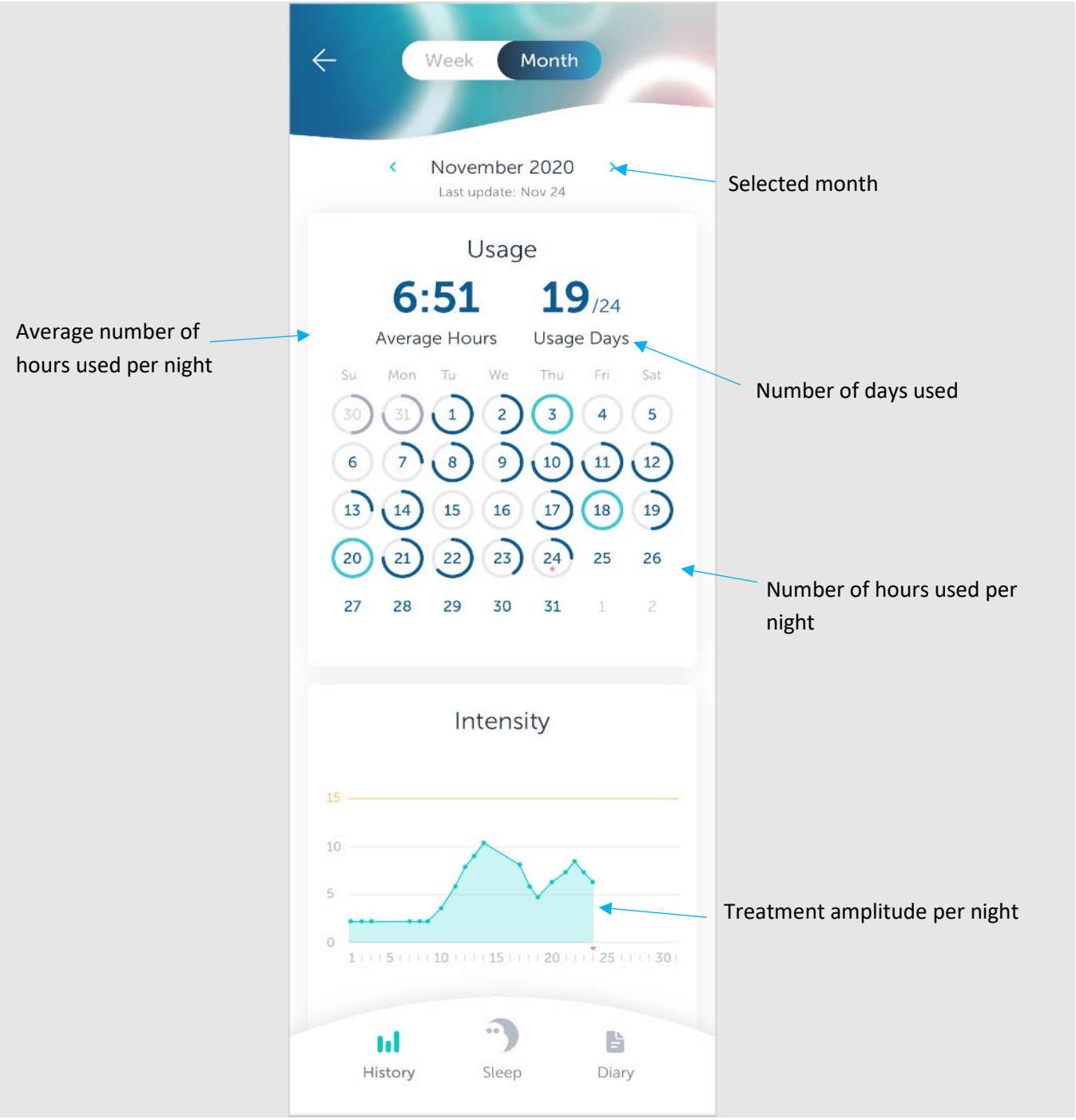
The weekly usage history tab includes the following information:

- Number of days the system was used within the selected timeframe.
- Average number of hours the system was used per night over the duration of the selected timeframe.
  Note: The average hours of use per night does not include the duration of delay and pause periods, but only when stimulation was delivered.
- A graphical representation of the number of hours used per night over the selected timeframe, either blue or green depending on whether you reached the default target duration of seven hours.
- The stimulation intensity set each night during the selected timeframe.
  Note: If the stimulation intensity was changed during the night, the last chosen intensity will be displayed in the log.



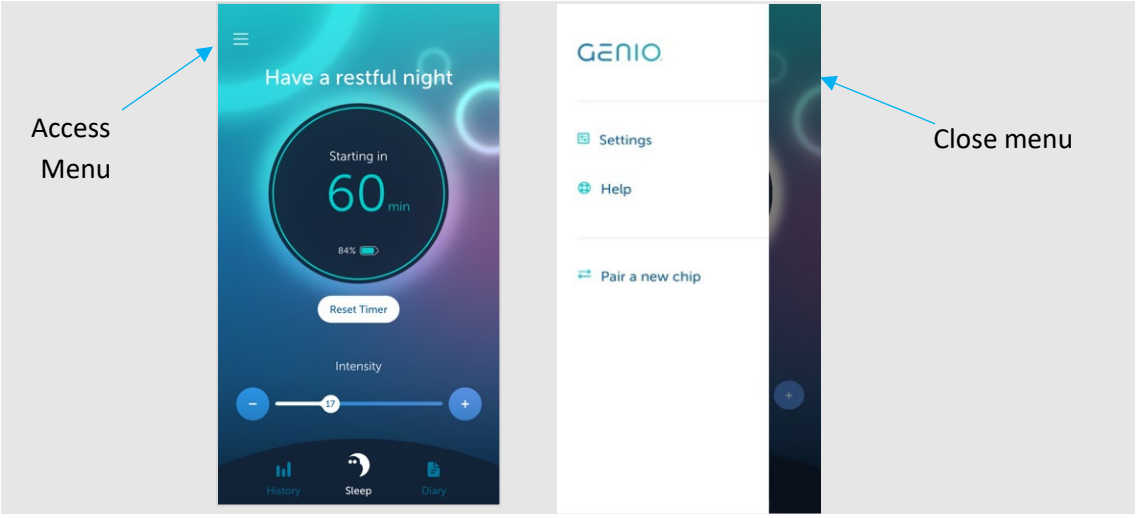
The monthly usage history tab includes the following information:

- Number of days the system was used that month.
- Average number of hours the system was used per night that month.
  Note: The average hours of use per night does not include the duration of delay and pause periods, but only when stimulation was delivered.
- A graphical representation of the number of hours used per night over the selected timeframe, either circled in blue or green depending on whether you reached the default target duration of seven hours.
- The stimulation intensity set each night during the selected timeframe.



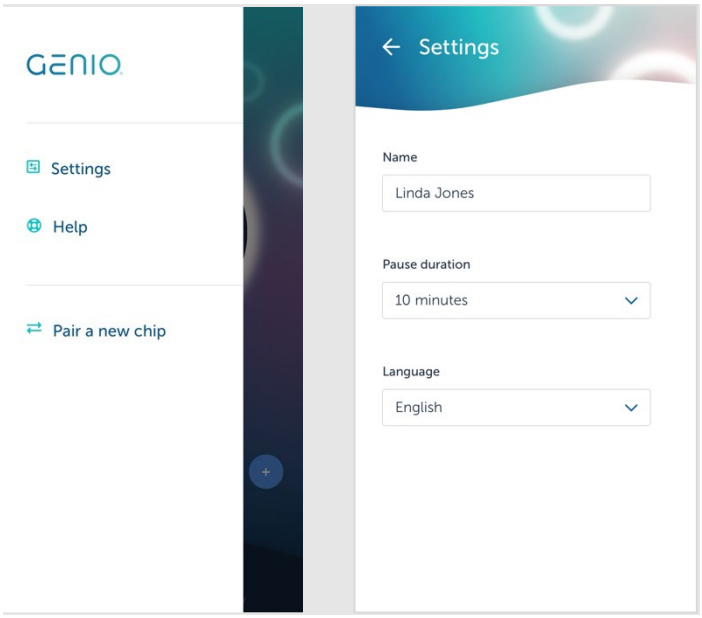
6.3. The Genio® Smartphone Application Main Menu

The Smartphone Application main menu can be accessed by clicking on the “Menu” symbol and enables access these sections, detailed in the following: settings, notifications, help and pair a new chip. To close the menu and go back to the main screen of the Smartphone Application, click on the “Menu” symbol.



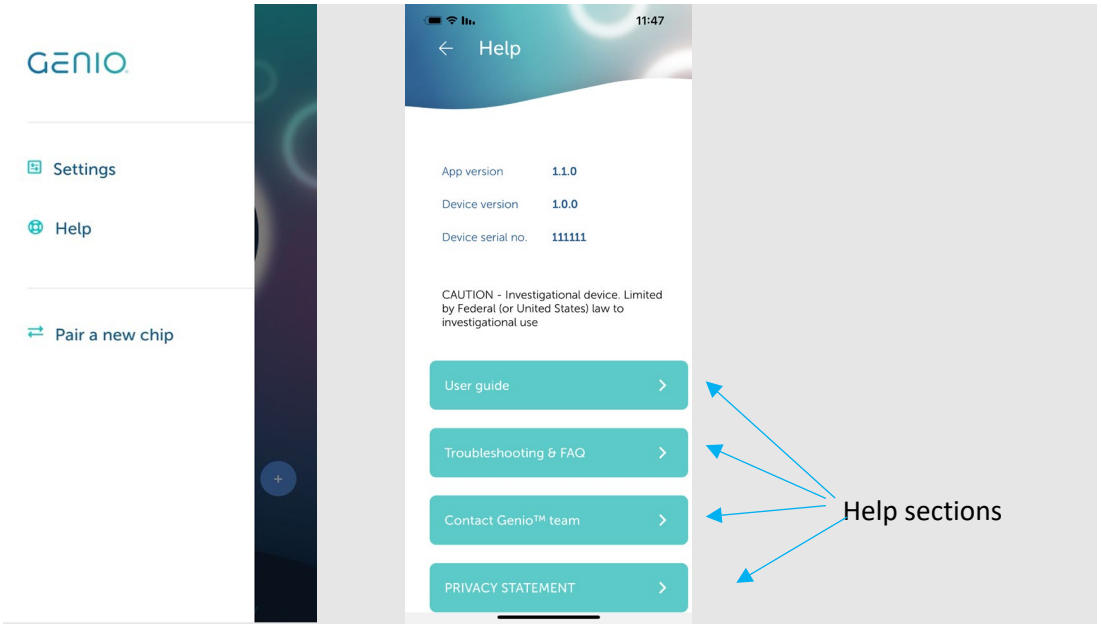
6.3.1. Settings

The settings screen allows you to 1) modify your username, 2) define your preferred pause duration and 3) change the Smartphone Application language.



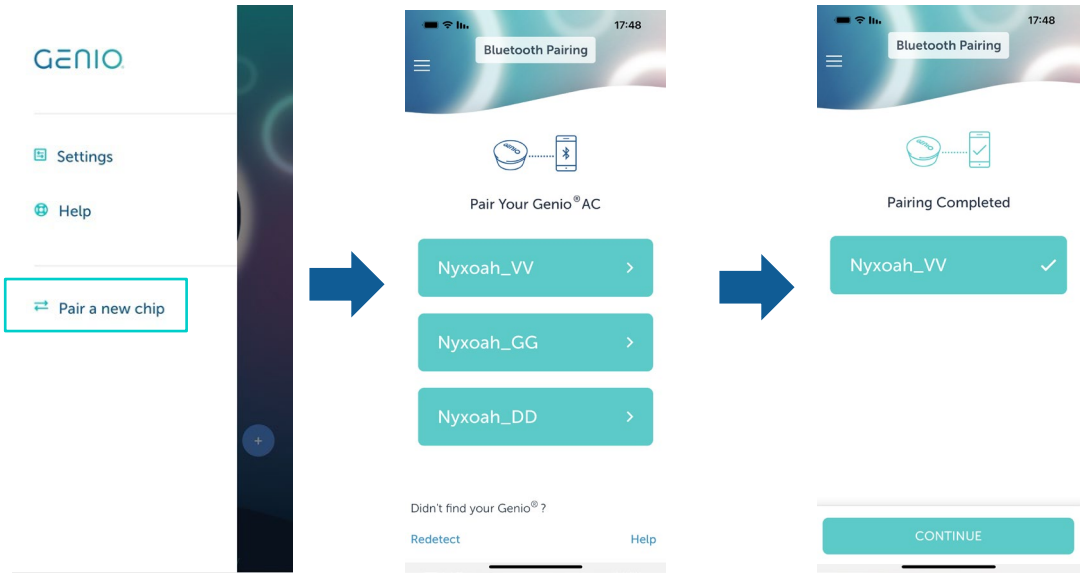
6.3.2. Help

The Help screen includes device information such as the Smartphone Application version, the Activation Chip version and serial number, and links to the user guide, a troubleshooting section, a frequently asked questions (FAQ), and a form to contact the Genio® team, and the Privacy Statement.



6.3.3. Pairing a new Activation Chip

When receiving a new Activation Chip, you will need to pair it with your Smartphone Application. Go to the Menu, select “Pair a new chip”, select the relevant chip in the list and wait until pairing is completed.



7. Troubleshooting

This section details troubleshooting for the Genio® System 2.1. If your question or problem is not answered below, contact your health care provider.

Note: A summary of the light indications of the devices is available in Section 8 "Visual Indications".

7.1. General Troubleshooting for the Genio® System 2.1

7.1.1. I did not use the Genio® System 2.1 for one or several nights

If you did not apply the Disposable Patch and Activation Chip for one or several nights, start applying them each night starting immediately.

7.1.2. The tongue stimulation began before I fell asleep

If you feel that your tongue is being stimulated before you fall asleep, consult your health care provider. The delay time to turn on the stimulation may be adjusted accordingly. If you require more time to fall asleep prior to adjustment of the delay time, place the Activation Chip in the docking area of the Charging Unit to reset the Activation Chip and activate a second period of delay time. If you are using the Genio® Smartphone Application, the delay timer can be reset by pressing the "Reset Timer" button on the main screen.

7.1.3. I felt discomfort when using the Genio® System 2.1

If you experience any discomfort with the Genio® System 2.1, consult your health care provider at the earliest opportunity. If this uncomfortable sensation prevents you to sleep, stop using the system until you have consulted your health care provider.

7.1.4. I woke up during the night and wanted to fall back asleep without feeling the stimulation

If you wake up during the night and want to start the delay time again and fall asleep without feeling the stimulation, follow these steps:

- **Step 1 -** Carefully disconnect the Activation Chip from the Disposable Patch by holding the patch with your fingers to avoid patch detachment.
- **Step 2 -** Place the Activation Chip in the docking area of the Charging Unit.
- **Step 3 -** Take out the Activation Chip from the Charging Unit and ensure the red, yellow and green lights are displayed on the Activation Chip.
- **Step 4 -** Ensure the light on the Activation Chip is blinking (green or yellow) and reconnect the Activation Chip to the Disposable Patch. The stimulation will resume following the programmed delay time.

Alternatively, if you are using the Genio® Smartphone Application, stimulation can be paused using the app, and stimulation will resume after an additional delay period.

7.1.5. I woke up during the night and wanted to stop the stimulation

If you wake up during the night and want to temporarily pause stimulation, follow these steps:

Step 1 - Carefully disconnect the Activation Chip from the Disposable Patch by holding the patch with your fingers to avoid patch detachment.

Step 2 - Place the Activation Chip in the docking area of the Charging Unit.

Step 3 - When going back to sleep, take out the Activation Chip from the Charging Unit and reconnect the Activation Chip to the Disposable Patch. The stimulation will resume following the programmed delay time.

Alternatively, if you are using the Genio® Smartphone Application, stimulation can be paused using the app, and stimulation will resume after an additional delay period.

Make sure the Activation Chip is properly attached to the Disposable Patch and that the patch is still correctly attached to the skin. In case the patch is not fully attached anymore, take a new one and replace it.

If you want to remove the Disposable Patch during the night, please follow these steps:

Step 1 - Remove the Disposable Patch and the Activation Chip from your chin.

Step 2 - Disconnect the Activation Chip from the Disposable Patch and discard the used Disposable Patch.

Note: It is recommended that all used Disposable Patches be brought to an electronic waste recycler as they contain printed circuit boards which should not be landfilled.

Step 3 - Place the Activation Chip in the docking area of the Charging Unit.

Step 4 - When going back to sleep, connect the Activation Chip to a **new** Disposable Patch.

Step 5 - Peel off the adhesive liner of the new Disposable Patch.

Step 6 - Correctly position the Disposable Patch and Activation Chip under your chin as instructed in section “Using your Genio® System 2.1”. The stimulation will start again following the programmed delay time.

7.1.6. I woke up during the night and I did not feel any stimulation

If you wake up during the night and do not feel any stimulation, follow these steps:

Step 1 - Carefully disconnect the Activation Chip from the Disposable Patch by holding the patch with your fingers to avoid patch detachment.

Step 2 - Place the Activation Chip in the docking area of the Charging Unit.

Step 3 - Take out the Activation Chip from the Charging Unit.

The Activation Chip light should blink red, yellow and green, and then blink slowly (green or yellow) to indicate it is ready to be attached to a patch.

Step 4 - Reconnect the Activation Chip to the Disposable Patch. Make sure the Activation Chip is properly connected and that the Disposable Patch is still correctly attached to the skin. Upon connection, you should feel a confirmation pulse indicating the Activation Chip is properly connected to the Disposable Patch.

Step 5 - If you do not feel that confirmation pulse, report this problem to your health care provider at the earliest opportunity.

7.2. Troubleshooting the Activation Chip

7.2.1. The light of the Activation Chip did not turn red, yellow and green when removing it from the Charging Unit

If you remove the Activation Chip from the Charging Unit and the Activation Chip light does not blink red, yellow and green:

Step 1 - Place the Activation Chip in the docking area of the Charging Unit. If the Activation Chip green light blinks, it means that the Activation Chip was not fully charged for use. The Activation Chip may take up to three hours to fully charge.

Step 2 - If the Activation Chip green light does not blink or turn on, verify that the green lights on the Charging Unit and power adapter are on. If the problem persists, it may signify a potential security risk .Report this to your health care provider at the earliest opportunity.

7.2.2. The red light of the Activation Chip blinked slowly after reset

If the red light on the Activation Chip slowly blinks for a few seconds after being reset in the Charging Unit, meaning after the red/yellow/green lights appeared, this indicates that the Activation Chip is malfunctioning. If this occurs, you should stop using your Genio system and should report this problem to your health care provider at the earliest opportunity in order to get a new Activation Chip.

7.2.3. The red light of the Activation Chip blinked slowly 2 minutes after connection to the Disposable Patch

If you did not attempt to pair the Activation Chip with your smartphone and notice the red light blinking slowly 2 minutes after connecting to the Disposable Patch, this could signify a potential security risk. In this case, it is recommended to temporarily discontinue use and report this problem to your health care provider to receive instructions on continuation of use.

7.2.4. No blinking light was displayed on the Activation Chip when I was about to attach it to a Disposable Patch

If no light is blinking on the Activation Chip when you are about to attach it to a Disposable Patch:

Step 1 - Ensure the green light on the Charging Unit is on and place the Activation Chip in the docking area of the Charging Unit.

Step 2 - Take out the Activation Chip from the Charging Unit. The Activation Chip light should blink (red, yellow and green) and then blink slowly to indicate it is ready to be connected to a patch.

Step 3 - If the red/yellow/green lights are not displayed by the Activation Chip, repeat step 1 and verify that the green light on the Activation Chip is constantly on. If the green light on the chip is blinking, it means your Activation Chip needs to be recharged prior to being used. Leave it in the Charging Unit for charging and then try again. If problem persists after completing these steps report the problem to your health care provider at the earliest opportunity.

7.2.5. No light appeared on the Activation Chip when I connected it to the Disposable Patch

If you connect the Activation Chip to the Disposable Patch and the light of the Activation Chip does not shine:

Step 1 - Disconnect the Activation Chip from the Disposable Patch.

Step 2 - Ensure the green light on the Charging Unit is on and place the Activation Chip in the docking area of the Charging Unit.

Step 3 - Take out the Activation Chip from the Charging Unit. The Activation Chip light should shine (red, yellow and green) and then blink slowly for a few seconds, indicating it is ready to be connected to a patch.

Step 4 - If Steps 1-3 did not resolve the issue, place the Activation Chip in the Charging Unit and leave it to charge until battery is fully charged, then repeat Step 3.
If problem persists, report the problem to your health care provider at the earliest opportunity.

7.2.6. The Activation Chip was dropped or suffered damage

If the Activation Chip is dropped or appears damaged, report the problem to your health care provider at the earliest opportunity.

7.2.7. I had difficulties removing the Activation Chip from its protective cover

Refer to section “Installing your Genio® System 2.1”, Step 3 for instructions on how to carefully remove the Activation Chip from its protective cover. If the Activation Chip was dropped or suffered damaged during these steps, report the problem to your health care provider at the earliest opportunity.

7.2.8. I had difficulties disconnecting the Activation Chip from the Disposable Patch during the night to perform a reset

If you often need to reset the Activation Chip during the night, you might have difficulties disconnecting the chip from the patch. To ease this process, prior to going to sleep, follow the instructions detailed in section “Using your Genio® System 2.1” but once you have connected the Activation Chip to the Disposable Patch, disconnect it and then reconnect it. This action will make the clip of the patch a bit more flexible, therefore making the Activation Chip reset easier.

7.3. Troubleshooting the Charging Unit

7.3.1. I left the Activation Chip in the Charging Unit even though the Activation Chip light indicates that the chip was fully charged

The Activation Chip can be left in the Charging Unit even if it is already fully charged. It is recommended to keep the Activation Chip in the Charging Unit all day until the next use.

7.3.2. The light of the Charging Unit did not turn on when connected to the power adapter

If the Charging Unit light does not turn on when connected to the power adapter:

Step 1 - Check that the power adapter is properly connected to power outlet and that the green light on the power adapter is on.

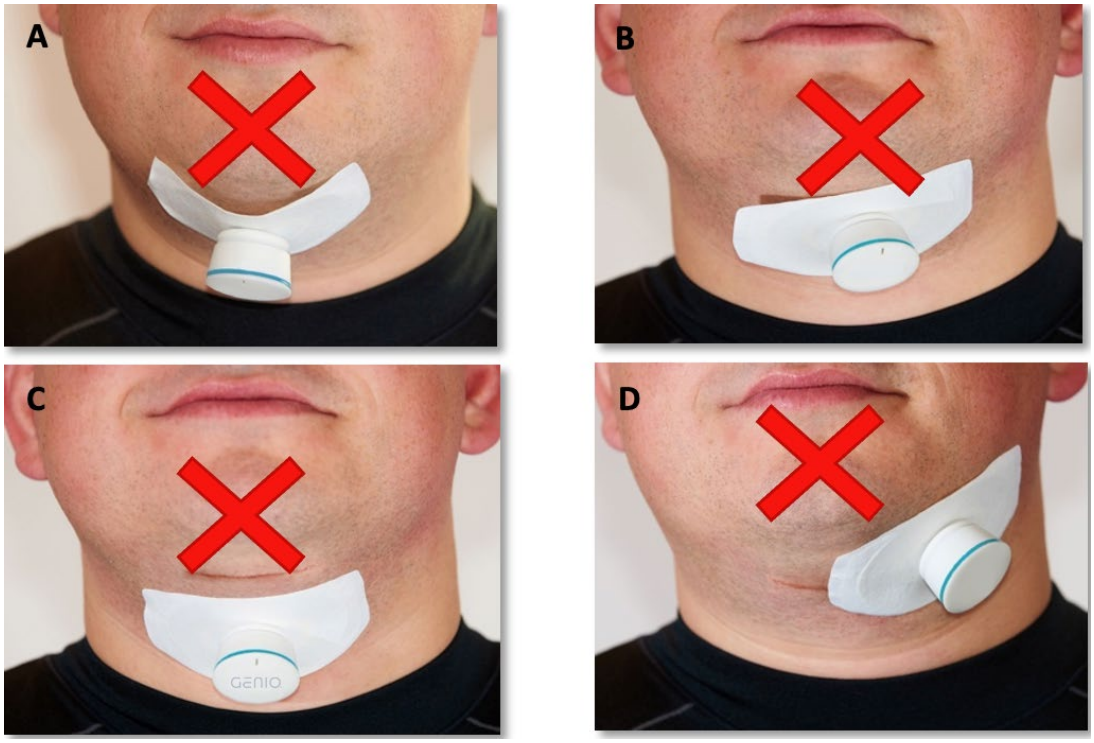
Step 2 - Verify that the power adapter cable is properly connected to the Charging Unit.

Step 3 - If the light of the Charging Unit still does not turn on, report the problem to your health care provider at the earliest opportunity.

7.4. Troubleshooting the Disposable Patch

7.4.1. I am not sure I placed the Disposable Patch correctly

The following shows how **NOT** to position the Disposable Patch. If you have positioned it in one of these ways, then simply remove it carefully and apply a **new** one correctly. Refer to section "Using your Genio® System 2.1", steps 5 and 6 for correct placement.



Incorrect positions of the Disposable Patch. (A) Center of the Disposable Patch not fully attached to the skin. (B) Border of the Disposable Patch not fully attached to the skin. (C) Disposable Patch positioned too low (on the neck). (D) Disposable Patch not aligned with the center of chin.

7.5. Troubleshooting the Genio® Smartphone Application

7.5.1. My history screen is empty

If your Genio® history is empty even though it is not the first time you are using your Genio® Smartphone App, follow these steps:

1. Reset your Activation Chip by placing it in the Charging Unit docking area and removing it.
2. Make sure that the Activation Chip is sufficiently charged. If not sufficiently charged, recharge your Activation Chip and try again once fully charged.
3. Connect the Activation Chip to a Disposable Patch and make sure to place it close to your smartphone before refreshing the usage history.
   If the problem persists, contact Nyxoah.

7.5.2. I adjusted the stimulation intensity during the delay time and could feel the stimulation

When the stimulation intensity is modified during the delay time, you will feel a single stimulation train after each adjustment to allow you to assess the suitability of the selected intensity before going to sleep.

7.5.3. The delay time is over, but I cannot feel the stimulation

If the delay time is over, and you cannot feel the stimulation:

1. Try to increase the intensity of the stimulation by pressing the + button on the Smartphone Application.
2. If your Activation Chip is not detected by the Smartphone Application, it might mean that your Activation Chip is in deep sleep. Reset your Activation Chip in the Charging Unit, reconnect it to your Disposable Patch and verify your Activation Chip is detected by the Smartphone Application.
3. If you have reached the maximal intensity available and the problem persists, contact Nyxoah.

7.5.4. I am unable to pause stimulation using the Smartphone Application

If you are unable to pause stimulation using the Smartphone Application, remove the Activation Chip from the Disposable Patch to stop stimulation immediately.

7.5.5. I am having issues with the wireless communication between the Activation Chip and the Smartphone Application

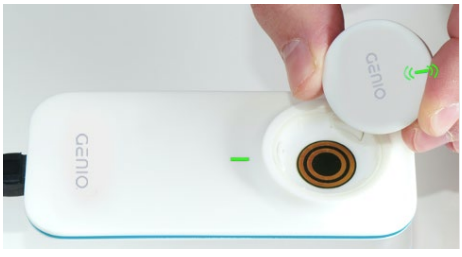
Communication Interference between the Smartphone Application and the Activation Chip may be caused temporarily by other wireless devices or proximity of your Activation Chip to large metallic surfaces. To reduce or stop interference, move away from the source. The effect is temporary and will not damage your device.

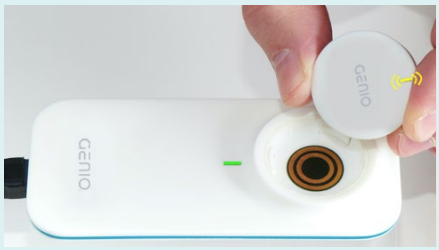
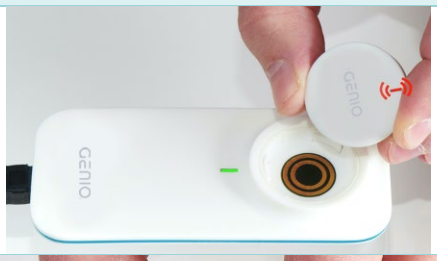
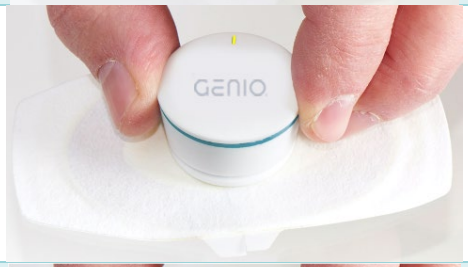
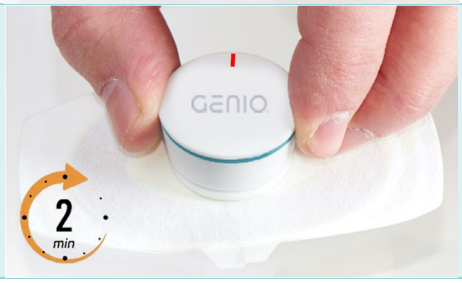
If you experience wireless communication issues between your Smartphone Application and your Activation Chip, the following troubleshooting steps should be performed:

1. Verify that Bluetooth is activated in your Smartphone settings
2. Verify that the Activation Chip is paired to your Smartphone by finding it in the Bluetooth devices connected to the Smartphone in the Bluetooth settings on your Smartphone
3. Verify that the Activation Chip is charged, connected to a Disposable Patch, and located close to your Smartphone
4. Verify that the Activation Chip and Disposable Patch are not located near large metallic surfaces
5. Verify that your Activation Chip is not located near other Bluetooth devices

After performing the above steps, you should retry using the Smartphone Application. If you continue to have issues with the wireless communication between the Activation Chip and the Smartphone Application, contact Nyxoah.

8. Visual Indications

Light indication	Meaning	Visual
Steady green light on power adapter	The power adapter is properly connected to power	
Steady green light on Charging Unit	The Charging Unit is properly connected to power	
Blinking green light on Activation Chip (while connected to the Charging Unit)	The Activation Chip is charging	
Steady green light on Activation Chip (while connected to the Charging Unit)	The Activation Chip is fully charged	
Red, yellow and green light sequence on Activation Chip	The Activation Chip is resetting	
Blinking green light on Activation Chip (after removal from the Charging Unit)	The Activation Chip is fully charged and ready to be connected to a Disposable Patch	

Light indication	Meaning	Visual
Blinking yellow light on Activation Chip (after removal from the Charging Unit)	The Activation Chip is not fully charged but can be connected to a Disposable Patch	
Blinking red light on Activation Chip (after removal from the Charging Unit)	The Activation Chip is malfunctioning and cannot be used	
Steady green light on Activation Chip (after connection to the Disposable Patch)	The Activation Chip is properly connected to the Disposable Patch and is fully charged	
Steady yellow light on Activation Chip (after connection to the Disposable Patch)	The Activation Chip is properly connected to the Disposable Patch but is not fully charged	
Blinking red light on Activation Chip (2 minutes after connection to the Disposable Patch)	Incorrect pairing code was entered. The Activation Chip cannot be used until resetting it	

9. Warranty Information

Your Genio® System 2.1 components are covered under a limited warranty. If any of your Genio® System 2.1 components stop functioning during your continued use of Genio® therapy, Nyxoah will replace it free of charge within the warranty period. Information on the warranty period for each of the Genio® System 2.1 components is as follows:

Genio® System 2.1 Component	Warranty Period
Implantable Stimulator	3 years
Activation Chip	1 year
Charging Unit	1 year
Disposable Patch	Any product which malfunctions and is not past its use-by date will be replaced by Nyxoah

If you experience any issues with your Genio® System 2.1 components, please contact your healthcare provider or Nyxoah for further instructions.

10. Cybersecurity

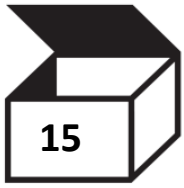
- The Genio® System is designed to reduce cybersecurity threats and minimize the system's vulnerability to cybersecurity attacks.
- Communication between your Activation Chip and Smartphone Application is based on Bluetooth Low Energy (BLE) and requires a passcode protected pairing and bonding of the devices before use. Communication is protected by data encryption (ECDHE) to reduce cyber security related threats.
- Communication between the Smartphone Application and Activation Chip requires the devices to be in proximity to each other. The Activation Chip cannot be controlled remotely.
- No sensitive data is stored on any component of the Genio® System, including the Smartphone Application.
- Never try to connect any Genio® System devices with cellular applications other than the Nyxoah certified application from the App Store or Google Play (on Android devices).
- The Smartphone Application is designed to operate on the following Operating Systems:
    - iOS versions 13 and above
    - Android versions 10 and above.
- As the Smartphone Application enables controlling the stimulation intensity of the Activation Chip, in order to reduce cybersecurity threats during use of the system, it is recommended that you consider adding password protection for your Smartphone in order to prevent unauthorized stimulation intensity changes which may result in temporary discomfort.Nyxoah performs ongoing monitoring and maintenance of product cybersecurity vulnerabilities. If Nyxoah becomes aware of a cybersecurity compromise, or the availability of cybersecurity patches and upgrades for the devices, users will be notified of this information via the Nyxoah website and/or direct customer notifications.
- Contact Nyxoah if you believe there is or has been a potential security risk to your product.

11. Symbols on Product or Package Labeling

Symbol/Title	Explanatory Text	Standard/Reference Number
 Manufacturer	Indicates the manufacturer of the medical device	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.1] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [3082]
 Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.6] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2493]
 Serial number	Indicates the serial number of the medical device to allow for identification	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.7] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2498]
 Batch code	Indicates the batch code so that the batch or the lot of the medical device can be identified. Other synonyms for "batch code" are "lot number", "lot code" and "batch number"	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.5] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2492]
 Date of manufacture	Indicates the date when the medical device was manufactured	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.3] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2497]
 Use-by date	Indicates the date after which the medical device is not to be used. Other synonyms for "use-by date" are "use by", "expiry date" and "expiration date"	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.1.4] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2607]

Symbol/Title	Explanatory Text	Standard/Reference Number
 Follow instructions for use	Indicates that reading the instruction manual prior to operating the device is mandatory	IEC 60601-1:2005/A1:2012 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [Table D.2, Symbol 10] ISO 7010:2019 – Graphical symbols – Safety colours and safety signs – Registered safety signs [M002]
 Caution	Indicates that caution is necessary when operating the device or control close to where the symbol is placed, or that the current situation needs operator awareness or operator action in order to avoid undesirable consequences	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.4.4] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [0434A]
 Sterilized using ethylene oxide	Indicates that the medical device has been sterilized using ethylene oxide	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.2.3] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2501]
 Do not use if package is damaged and consult instructions for use	Indicates that the medical device 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 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.2.8] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2606]
 Do not resterilize	Indicates that the medical device is not to be resterilized	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.2.6] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2608]
 Do not re-use	Indicates that the medical device is intended for one single use only	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.4.2] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [1051]

Symbol/Title	Explanatory Text	Standard/Reference Number
 Keep away from sunlight	Indicates that the medical device needs protection from light sources	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.3.2] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [0621]
 Keep dry	Indicates that the medical device needs to be protected from moisture	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.3.4] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [0626]
 Temperature limit	Indicates the temperature limits to which the medical device can be safely exposed	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.3.7] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [0632]
 Humidity limitation	Indicates the range of humidity to which the medical device can be safely exposed	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.3.8] ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2620]
 Magnetic Resonance (MR) Conditional	Indicates 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	ASTM F2503-20 – Standard Practice For Marking Medical Devices And Other Items for Safety In The Magnetic Resonance Environment [3.1.11]
 Prescription Use Only	Indicates that Federal (USA) law restricts the device to sale by or on the order of a licensed physician	United States Code of Federal Regulations; 21 CFR 801.109(b)(1)

Symbol/Title	Explanatory Text	Standard/Reference Number
 Class II Equipment	Identifies equipment which meets the safety requirements specified for Class II equipment (double insulated equipment)	IEC 60417:2002 – Graphical symbols for use on equipment [5172] IEC 60601-1:2005/A1:2012 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [Table D.1, Symbol 9]
 Non-ionizing electromagnetic radiation	Indicates medical electrical equipment that includes RF transmitters or that intentionally apply RF electromagnetic energy for diagnosis or treatment	IEC 60417:2002 – Graphical symbols for use on equipment [5140]
 Type BF applied part	Identifies a type BF applied part (a part which is generally not conductive and can be immediately released from the patient)	IEC 60417:2002 – Graphical symbols for use on equipment [5333] IEC 60601-1:2005/A1:2012 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [Table D.1, 20]
 FCC Mark	Indicates that the electromagnetic radiation of the device is below the limits specified by the Federal Communications Commission	United States Code of Federal Regulations; Title 47
IP21 Degrees of protection provided by enclosures	Indicates that the device is protected against the ingress of solid objects over 12.5mm and protected against ingress of vertically dripping water	IEC 60601-1:2005/A1:2012 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [Table D.3, Symbol 2]
IP22 Degrees of protection provided by enclosures	Indicates that the device is protected against the ingress of solid objects over 12.5mm and protected against ingress of dripping water at any angle up to 15 degrees from vertical	IEC 60601-1:2005/A1:2012 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [Table D.3, Symbol 2]
 Quantity in box	Indicates the amount of devices contained within the box	ISO 7000:2019 – Graphical symbols for use on equipment – Registered symbols [2794]

Symbol/Title	Explanatory Text	Standard/Reference Number
UDI Unique device identifier	Indicates a carrier that contains unique device identifier information	ISO 15223-1:2021 – Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements [5.7.10]
 Waste electrical and electronic equipment	Indicates that the disposal of the device requires separate collection in the European Union	Directive 2012/19/EU on waste electrical and electronic equipment (WEEE)

12. Electromagnetic Compatibility Requirements

12.1. Use environment

The Genio® System 2.1 (Activation Chip, Disposable Patch, Implantable Stimulator, Power Adapter and Charging Unit parts) is intended for use in a home healthcare environment.

12.2. Essential Performance

The following table lists the Genio® System 2.1 essential performance functions per system component:

Device	Essential performance functions
Implantable Stimulator	Delivering stimulation pulses according to 8 MHz electromagnetic field transmitted from an external device (Activation Chip or External Stimulator)
Activation Chip and Disposable Patch	Transmission of modulated 8 MHz EM field to power the Implantable Stimulator
Activation Chip	Activation and handling of BLE interface Charging Activation Chip battery
Charging Unit and Power Adapter	Charging Activation Chip battery

12.3. Wireless Functions

System component	Specific RF wireless type	Type	Wireless functions
Implantable Stimulator	Wireless modulated energy transfer 8 MHz	Receiver	Receiving stimulation energy and pattern from the Activation Chip -Disposable Patch
Activation Chip - Disposable Patch	Wireless modulated energy transfer 8 MHz	Transmitter	Energy transfer to the Implantable Stimulator
	BLE (Bluetooth Low Energy) 2.4 GHz	Transceiver	Communication and data transfer between the Activation Chip and Smartphone Application software
Genio® Smartphone Application	BLE (Bluetooth Low Energy) 2.4 GHz	Transceiver	Communication and data transfer between the Activation Chip and Smartphone Application software

12.3.1. Wireless Communication between the Activation Chip and the Genio® Smartphone Application

Communication Interference between the Smartphone Application and the Activation Chip may be temporarily disturbed by other wireless devices or large metallic surfaces located near your Activation Chip. To reduce or stop interference, move away from the source. The effect is temporary and will not damage your device. See Section 7.5.5 for additional troubleshooting information.

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: "Harmful interference" is defined in 47 CFR §2.122 by the FCC as follows: Interference which endangers the functioning of a radionavigation service or of other safety services or seriously degrades, obstructs, or repeatedly interrupts a radio communication service operating in accordance with the [ITU] Radio Regulations

12.4. Electromagnetic Compatibility (EMC) Warnings

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

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

WARNING: Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the Genio® System 2.1, including cables specified by Nyxoah. Otherwise, degradation of the performance of this equipment could result.

WARNING: The Genio® System 2.1 needs special precautions regarding EMC and needs to be installed and put into service according to the specific instructions for maintaining basic safety and essential performance with regard to electromagnetic disturbances for the expected service life provided in sections 2 and 3.

12.5. Power Inputs and Frequencies

The following table lists the Genio® System 2.1 devices power inputs and Radio frequencies (if applicable):

Device	Power Inputs	Radio Frequencies
Activation Chip + Disposable Patch	4.2 V, 160 mAh (Battery Powered)	8 MHz BLE: 2.4 GHz
External Stimulator	3.7 V, 120 mAh (Battery Powered)	8 MHz
Charging Unit	110-240 V, AC 50-60 Hz	N/A

12.6. EMC Guidance Tables

12.6.1. Guidance and manufacturer's declaration – electromagnetic emissions IEC 60601-1-2 Ed.4.1

Emissions test	Compliance	Electromagnetic environment - guidance
RF emissions CISPR 11	Group 1	The Genio® System 2.1 uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment
RF emissions CISPR 11	Class B	The Genio® System 2.1 is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/flicker emissions IEC 61000-3-3	Complies	

12.6.2. Guidance and manufacturer's declaration – Electromagnetic Immunity IEC 60601-1-2 Ed.4.1

Immunity test	IEC 60601 level	Compliance level	Electromagnetic environment - guidance
Electrostatic discharge (ESD), IEC 61000-4-2	8 kV contact 15 kV air	8 kV contact 15 kV air	The relative humidity should be at least 5%.
Electrical fast transient/burst, IEC 61000-4-4	2 kV for power supply lines 1 kV for SIP/SOP lines	2 kV for power supply lines 1 kV for SIP/SOP lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge, IEC 61000-4-5	1 kV line to line 2 kV line to earth	1 kV line to line (class II ME equipment and ME systems according to Table 5, note "k" of EN/IEC 60601-1-2)	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips and interruptions on power supply input lines IEC 61000-4-11	0 % U_T for 0.5 cycle 0 % U_T for 1 cycle 70 % U_T for 25/30 cycles 0 % U_T for 250/300 cycles	0 % U_T for 0.5 cycle 0 % U_T for 1 cycle 70 % U_T for 25/30 cycles 0 % U_T for 250/300 cycles	Mains power quality should be that of a typical commercial or hospital environment. If the user of the equipment requires continued operation during power mains interruptions, it is recommended that the equipment be powered from an uninterruptible power supply or a battery.
Power frequency magnetic field, IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Immunity to proximity magnetic fields IEC 61000-4-39	30KHz 8 A/m 134.2KHz 65 A/m 13.56MHz 7.5 A/m	30KHz 8 A/m 134.2KHz 65 A/m 13.56MHz 7.5 A/m	30KHz 8 A/m 134.2KHz (2.1KHz modulated) 65 A/m 13.56MHz (50KHz modulated) 7.5 A/m
NOTE: U_T is the AC mains voltage prior to application of the test level.			

12.6.3. Guidance and manufacturer's declaration – electromagnetic IMMUNITY IEC 60601-1-2 Ed.4.1

Immunity test	IEC 60601 level	Compliance level
IEC 61000-4-6 Conducted RF	3 Vrms 150 kHz to 80 MHz 6 Vrms in ISM bands (6.765 MHz to 6.795 MHz; 13.553 MHz to 13.567 MHz; 26.957 MHz to 27.283 MHz; and 40.66 MHz to 40.70 MHz) and amateur radio bands (1.8 MHz to 2.0 MHz, 3.5 MHz to 4.0 MHz, 5.3 MHz to 5.4 MHz, 7 MHz to 7.3 MHz, 10.1 MHz to 10.15 MHz, 14 MHz to 14.2 MHz, 18.07 MHz to 18.17 MHz, 21.0 MHz to 21.4 MHz, 24.89 MHz to 24.99 MHz, 28.0 MHz to 29.7 MHz and 50.0 MHz to 54.0 MHz)	[*V*] = 3 Vrms [*V*] = 6 Vrms
IEC 61000-4-3 Radiated RF	10 V/m 80 MHz to 2.7 GHz	[*E*] = 10 V/m
Proximity fields from RF wireless communications equipment	385 MHz	27 V/m
	450 MHz	28 V/m
	710 MHz	9 V/m
	745 MHz	
	780 MHz	
	810 MHz	28 V/m
	870 MHz	
	930 MHz	
	1720 MHz	28 V/m
	1845 MHz	
	1970 MHz	
	2450 MHz	28 V/m
	5240 MHz	9 V/m
	5500 MHz	
	5785 MHz	

12.7. RF Receivers and Transmitters Specifications

RF	Tx/Rx	Frequency, MHz	Assigned Frequency Range, MHz	Modulation	EIRP / Transmitter Power
Bluetooth	Tx/Rx	2400 [2402-2480]	2400-2483.5	GFSK	EIRP: -14.20 dBm (38 µW)
Power Transfer (External Stimulator)	Tx	8 [7.985-8.01125]	7.4-8.8	Per Treatment Protocol	H-Field strength: -2.88 dB(µA/m) (0.72 µA/m)
Power Transfer (Activation Chip - Disposable Patch)	Tx	8 [7.985-8.01125]	7.4-8.8	Per Treatment Protocol	H-Field strength: 34.7 dB (µA/m) (54.3 µA)

13. Index

This section includes keywords found throughout this Patient Manual which can help you to locate the information you may be looking for. If you are unable to find the answer to your question within this manual, please contact Nyxoah or your healthcare provider.