The Genio® System 2.1 Participant Manual

CAUTION - Investigational device. Limited by Federal (or United States) law to investigational use

Patented and design protected technology. Device not for sale in Europe, Australia or USA. For clinical use only.

Manufacturer Information:

NYXOAH SA
Rue Edouard Belin, 12
1435 Mont-Saint-Guibert
Belgium
Email: clinical@nyxoah.com
Phone: +32 (0)10 45 90 75

IDE Sponsor Information in the US:

NYXOAH, Inc
251 Little Falls Drive
Wilmington, DE 19808
United States of America
Email: clinical@nyxoah.com
Phone: 1-800 373-2605

IDE Sponsor Information in Europe:

NYXOAH SA
Rue Edouard Belin, 12
1435 Mont-Saint-Guibert
Belgium
Email: clinical@nyxoah.com
Phone: +32 (0)10 45 90 75

IDE Sponsor Information in Australia:

NYXOAH Pty Ltd
58 Gipps Street
Collingwood, VIC 3066
Australia
Email: clinical@nyxoah.com
Phone: +61 3 9419 7607

Contact Information

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

Sleep Specialist

Name:	
Phone Number:	

Implanting Hospital

Name:	
Address:	
Surgeon Name:	
Surgeon Phone Number:	

Participants, Family Members or Caregivers

Please be aware of the following:

- You should read this manual carefully before you start using the Genio® System 2.1. If you have any questions or problems, please refer to the “Troubleshooting” section. If your questions are not addressed in this user manual, please contact your doctor.
- You should always have your Participant Card with you and inform your doctor/s or any medical staff you have been implanted with the Genio® System 2.1 in the chin area. If they have any questions, doctors and medical staff can contact Nyxoah at the number provided in the sponsor information section (see page 2).
- If you experience any unusual symptoms or problems related to the use of your Genio® System 2.1, please report this to your doctor at your earliest convenience. Please refer to the Contact Information section (see page 3).

Table of Contents

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 participant, 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 participant 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 participant's snoring and sleep apnea.

EMC – Electromagnetic Compatibility

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. Refer to the "MRI Safety Information" in section 2 for more information.

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

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 participants 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 participant.

About this User Guide

You have received this manual because you have been implanted with a Genio® Implantable Stimulator, an investigational device, to treat moderate to severe Obstructive Sleep Apnea (OSA), in a clinical trial.

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

This user guide 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 user guide, or if any unusual situations or problems occur, contact your doctor.

1 Introduction

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.

About Your Genio® System 2.1

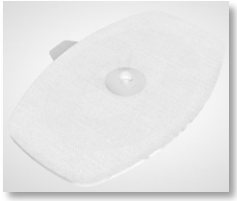
Your Genio® System 2.1 is made up of four main parts: The Implantable Stimulator, the Genio® Disposable Patch, the Genio® Activation Chip and the Genio® Charging Unit. Here is what each part of the system does:

The Genio® Implantable Stimulator is a small saddle-shaped implant that consists of a flat area enclosing the antenna and two "legs" with two metal pads each, called electrodes. This implant is implanted using a surgical procedure under the chin close to a nerve of 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 normal breathing during sleep.

The Genio® **Activation Chip** is the power source for the Implantable Stimulator. It will be programmed with the settings that provide the stimulation therapy that your physician has chosen for you and has a battery. You will be required to charge the Genio® Activation Chip daily.

The Genio® **Charging Unit** and its power adapter (also referred to as Power Supply or PS) are used to recharge the Genio® Activation Chip's battery.

The **Disposable Patch** is an adhesive patch placed on the skin under the chin. The Genio® Disposable Patch is snapped onto the Genio® Activation Chip. Once snapped together stimulation energy can be transmitted to the Genio® Implantable Stimulator.



2 Safety Information

Intended Use

You are enrolled in a clinical investigation involving the Genio® System 2.1 which is intended to treat patients diagnosed with moderate to severe Obstructive Sleep Apnea (OSA) as defined by having an Apnea-Hypopnea Index [AHI] of greater or equal to 15 and less than or equal to 65 events/hour, which is the number of pauses in breathing per hour while asleep.

The Genio® System 2.1 is an investigational device intended for adult patients who have not tolerated, have failed or refused Positive Airway Pressure (PAP) treatments. PAP failure is defined as an inability to eliminate OSA (AHI of greater than 15 despite PAP usage) and PAP intolerance is defined as:

a) inability to use PAP (less than 5 nights per week of usage; usage defined as 4 hours or more of use per night); or

b) unwillingness to continue to use PAP (for example, a participant returns the PAP system after attempting to use it).

Contraindications

The Genio® System 2.1 is contraindicated for:

- Subjects below 22 or above 75 years old
- Subjects with a Body Mass Index (BMI) above 32 kg/m^2
- Subjects with an AHI below 15 or over 65 events/hour
- Subjects with combined central and mixed apnea-hypopnea index > 25% of the total AHI
- Pregnant/breastfeeding women or women planning to become pregnant
- Subjects with any functional or structural problem that would impair the ability of a hypoglossal nerve stimulator to treat OSA
- Subjects with any medical illness or condition that contraindicates a surgical procedure under general anesthesia or that would prevent the implantation of the Implantable Stimulator or the placement of Activation Chip/Disposable Patch
- Subjects with coagulopathy or requiring anticoagulant medications (such as warfarin, clopidogrel (Plavix) or similar; prophylactic aspirin not exclusionary) that cannot be safely stopped in the perioperative period
- Subjects with major head and neck abnormalities narrowing the airway or the implantation site
- Subjects with hypersensitivity to any material of system components

Warnings

Pediatric Use

Safety and effectiveness of the use of the Genio® System 2.1 has not been established in children.

Components

The use of charging adapters not provided by Nyxoah may result in device malfunction, damaged devices or increase the risks to the users.

Changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate the equipment

Interaction with Other Active Implantable Medical Devices (AIMD)

You should not have other Active Implantable Medical Devices (AIMD) even if the devices can be temporarily turned off because they may interfere with the Genio® Implantable Stimulator, i.e. the potential for interference has not been studied. You should discuss with doctors involved in both therapies prior to surgery.

MRI Safety Information 

It is important that you read the information in this section and consult your treating physician if you were instructed to undergo an MR scan. This section contains important information regarding the Genio® Implantable Stimulator (IS) and the conditions in which you can safely undergo an MR scan.

Please share this information with your treating physician and MR technician, discuss having an MR scan with them and bring this manual and your participant card with you to the MR scan appointment. MR scans must be performed only as described in this section.

The Genio® IS is a Magnetic Resonance (MR) Conditional device marked by the following symbol 

which means that the implant is safe in the MR environment within certain conditions.

MR Scan Conditions

Non-clinical testing has demonstrated the Genio® IS is MR Conditional. A patient with this device can be safely scanned in an MR system meeting the following conditions:

- Static magnetic field of 1.5 Tesla and 3 Tesla, with:
  - Maximum spatial field gradient of 2000 G/cm (20 T/m)
  - Maximum switched gradient slew rate per axis of 200 mT/m/ms
  - Maximum switched gradient amplitude per axis of 45 mT/m
  - Maximum scan duration:

Landmark Position	Scan duration	Maximum SAR
Head/Neck/Thorax	<15 minutes continuous scanning	Whole body averaged specific absorption rate (SAR) of 1 W/kg or head averaged SAR of 1.6 W/kg (Normal Operating Mode)
Torso and Lower regions	<15 minutes continuous scanning	Whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode)

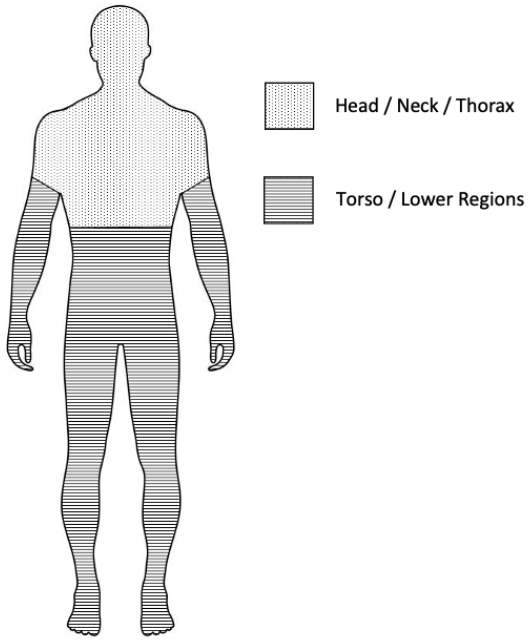


Figure 1: Scan Conditions (1.5T and 3T)

Under the scan conditions defined above, the Genio® Implantable Stimulator is expected to produce a maximum temperature rise of less than 5° C continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 5 cm from the Genio® Implantable Stimulator when imaged with a gradient echo pulse sequence and a 3 Tesla MR system.

Patient warnings and precautions

- Caution: In some instances, a stimulation of the tongue muscles can occur leading to uncomfortable sensation.
- Do not bring the Genio® System 2.1 external devices (such as the Genio® Disposable Patch or Genio® Activation Chip) with you to the MR scan room. The use of the Genio® Disposable Patch and Activation Chip during an MR scan is prohibited.
- Do not go through an MR scan if you have fever.
- The device may move and thus cause discomfort and/or pain when used in the scanner.
- You may feel uncomfortable pain or heating during part of or the entire MR scan. If you feel intolerable discomfort, notify the MR technician so that the scan can be stopped.
- The MR scan should be conducted at least 6 weeks after your implantation or revision surgery. If you are required to undergo an MR scan during this period, please consult your treating physician.
- In case you experience a change in implant functionality please contact your treating physician.

MRI Technician warnings and precautions

- Caution: In some instances, a stimulation of the tongue muscles can occur leading to uncomfortable sensation.
- Genio® System 2.1 external devices (such as the Genio® Disposable Patch or Genio® Activation Chip) shall not be brought by the patient to the MR scan room and used during the MR scan. The use of the Genio® Disposable Patch and Genio® Activation Chip during an MR scan is prohibited.
- Do not scan patients with fever.
- During the MR scan, continuously monitor the patient, notice any signs of anxiety and/or discomfort.
- The device may move and thus cause discomfort and/or pain when used with the scanner.
- The patient may feel discomfort during part or all of the MR scan. If the patient feels uncomfortable pain or heating which is intolerable, the scan should be terminated.
- The MR scan should be conducted at least 6 weeks after patient implantation or revision surgery.

Potential risks associated with MR scans

The Genio® IS device has been designed to minimize the potential adverse events that could result in patient harm.

The potential MR scan-related adverse events are listed below:

- Implant heating causing damage to tissue in contact with the implant

- Implant migration causing damage to tissue in contact with the implant
- Implant migration causing the implant to be surgically removed (and replaced)
- Unintended over stimulation causing damage to tissue in contact with the implant
- Unintended stimulation causing discomfort due to electrical stimulation
- Device malfunction causing the implant to be surgically removed (and replaced)
- Diagnostic problems due to artifacts - shadowing on the MR image in the vicinity of the implant causing loss or disturbance of diagnostic information

Precautions

Pregnancy

There might be unknown risks to pregnancy if the implanted device is used while pregnant. For this reason, you must inform your doctor if you are pregnant, breastfeeding or if you are planning to become pregnant. If you become pregnant after the implantation of the device, the device will need to be turned off as soon as possible. The device should remain OFF until you stop breastfeeding.

You are strongly advised to use effective contraception during the course of the study.

Defibrillation/Cardioversion

If you have a serious heart rhythm problem (such as ventricular or atrial fibrillation), the first consideration is your survival. If it happens while you are wearing the devices, the Disposable Patch and the attached Activation Chip should be removed from your chin prior to the use of defibrillation or cardioversion. After defibrillation or cardioversion, your doctor should confirm the Genio® System 2.1 is working as intended. Please note that possible interaction between the Genio® System 2.1 and cardiac devices (implantable defibrillators) has not been investigated.

Water and Humidity

You are advised to keep your Genio® external devices away from extremely humid areas and sources of water. Water and humidity may result in device malfunctions.

Medical Procedures

Always inform medical staff that you have been implanted with a medical device in the chin area before undergoing any medical procedures or examinations. The following medical procedures may interfere with the Genio® System 2.1 or cause permanent damage to your implant or to your body tissue. You should therefore consult your doctor prior to undergoing the following procedures:

- Treatment of muscle and joint conditions using heating of the tissue by high frequency electric current (diathermy)
- Treating abnormal heartbeats with an internal or external defibrillation
- Radiation therapy
- Treating kidney stones with ultrasound (lithotripsy)

- Magnetic stimulation, or any other form of electrical stimulation

Treatment with Therapeutic Ionizing Radiation

You should not undergo treatment with therapeutic ionizing radiation after the implantation of the Implantable Stimulator. If radiation therapy is required in the area of the device, the Genio® Implantable Stimulator might need to be surgically removed. If radiation therapy is applied to an area far away from the implanted device, the device should be shielded and its function confirmed after treatment.

Therapeutic Ultrasound

You should consult your doctor before undergoing treatment with ultrasound therapy as it might damage the Implantable Stimulator and/or might cause tissue damage.

Radio-Frequency or Microwave Ablation

You should not be exposed to radio-frequency or microwave ablation. The electrical current may cause heating resulting in device and/or tissue damage. If radio-frequency or microwave ablation is required in the area of the device, it might need to be surgically removed.

Hyperbaric Chambers

There may be possible safety hazards associated with hyperbaric chambers when you have the Implantable Stimulator in place. You should discuss the effects of high pressure with your doctor before entering hyperbaric chambers.

Entering Special Areas

Seek medical guidance before entering environments that are protected by a warning notice preventing entry by persons fitted with an Active Implantable Medical Device (AIMD) such as a pacemaker.

Metal Detectors

Interactions with metal detectors are unlikely to damage the Implantable Stimulator or cause clinically significant symptoms. However, the Implantable Stimulator contains metal parts that might possibly set off metal detector alarms. You must tell security personnel that you have an implanted device in the chin area and always have your Participant Card with you. Security wands should not affect the device.

Theft Detector, RFID systems and Security Screening Devices

Use care when approaching theft detectors, security devices and RFID systems (such as those found in airports, libraries, department stores, and government buildings). When approaching these devices, do the following:

1. Show the security personnel your Participant Card and notify them that you have an implanted medical device in your chin area.

2. If you must pass through the theft detector or security screening device or in proximity to RFID systems, proceed through the security device and keep as far from it as possible. Do not linger near or lean on such devices.

Note: Some theft detectors might not be visible.

Physical Activities and Sports

Use caution and consult your doctor prior to performing activities that may damage or displace your Implantable Stimulator such as diving, boxing, jack-hammering, extreme sports etc.

Participant Card

Carry your Participant Card with you at all times. This card supplies information about your Genio® System 2.1 and your doctor contact information. In case of a medical emergency or if you need to bypass security, present this card to security or medical personnel.

Device Charging

Your Activation Chip must be charged on a daily basis in order to be fully charged for the next night of use.

Cleaning your Devices

Participants shall ensure devices are kept in a clean environment. The Activation Chip should be kept in the provided protective cover when it is not in use or not being charged. Do not attempt to clean the devices. If functionality is compromised due to lack of cleanliness, please contact your physician.

Adverse Events

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 doctor. Risks of using the Genio® System 2.1 can be minimized by following this manual, and by following your doctor's instructions.

In addition to the risks described below, the device may have other risks that are currently unknown. You should immediately inform your doctor or a member of his/her team if you have any side effects, and you should inform them upon appearance of any other health issues. You should also inform them about any other treatments prescribed to you by doctors other than those caring for you in this study.

If a severe side effect or reaction occurs, your doctor may need to stop your therapy. Your doctor will discuss the best way of managing any side effects with you.

If you have any questions on these adverse events, consult your doctor.

Risks associated with the implantation procedure

For the purpose of device implantation, you will undergo a surgery procedure under general anesthesia. Whilst anesthesia is generally safe nowadays, there is always the possibility of some risks associated with anesthesia. The commonly known adverse events associated with

anesthesia are listed below. Most of these anesthesia-related events are uncommon and are generally resolved quickly. The risk of brain damage or death due to anesthesia is very low.

The risk of problems from anesthesia increases for people who have frequent surgical procedures within a short timeframe and participants with other high-risk diseases. If you have any concerns about these issues, you should discuss them with your doctor.

The anesthesia and implantation surgery may involve the following risks:

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

- Post-surgical discomfort
- Post-surgical numbness, tingling or other sensory changes related to the skin incision
- Post-surgical mild to moderate swelling or bruising around the incision site
- Post-surgical mild to moderate pain, stiffness or tenderness at the incision site
- Impaired or painful swallowing
- Impaired or painful speaking due to the procedure
- Paresthesia (sensation of ticking or itching)
- Bleeding (including hematoma)
- Abnormal scarring
- Pain or irritation in the throat or nasal passage from intubation
- Feeling unwell or vomiting
- Dry mouth
- Post-surgical hoarse voice due to anesthesia
- Bruising at the site of injections

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

- Post-surgical headache, dizziness
- Damage or trauma to nerves, blood vessels or muscles
- Transient tongue weakness
- Local skin irritation
- Post-surgical diarrhea
- Tongue fasciculations (twitching of tongue)
- Tongue muscle weakness or soreness
- Muscle or skin tightness
- Post-surgical back pain due to lying on the table during the procedure
- Infection

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

- Temporary lip weakness
- Post-surgical fever
- Superficial skin infection
- Impaired sense of taste
- Tongue may get larger or smaller
- Persistent pain at the implant site
- Post-surgical irritability, nervousness, confusion
- Post-surgical sleep problems like insomnia or sleepiness

- Post-surgical respiratory complications requiring ventilation
- Aspiration (i.e., food/fluid directed to windpipe when swallowing)
- Allergic reaction to anesthetics or other medications used before, during, or after the surgery

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 participants):

- Discomfort due to electrical stimulation
- Mild tongue abrasion
- Temporary local skin irritation
- Abnormal scarring
- Tongue fasciculations (twitching of tongue)
- Paresthesia (sensation of tickling or itching)
- Impaired or painful swallowing due to the device

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

- 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
- Mouth blisters (due to tongue rubbing against teeth during stimulation)
- Pain or irritation in the throat or nasal passage
- Post-surgical mild to moderate pain, stiffness or tenderness at the incision site
- Implant may need to be surgically removed (and replaced)
- Infection

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

- Allergic and/or rejection response to the implanted device
- Damage to tissue in contact with the implant
- Damage to tissue in contact with external devices
- Persistent pain at the implant site
- Impaired or painful speaking due to the device
- Damage or trauma to blood vessels/nerves in the vicinity of the implant
- Clinically significant implant migration (device moving from implanted location)
- Change in salivary flow

Risks associated with a revision surgery

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 a 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.

Risks associated with sleep studies

As part of this clinical study, you are required to participate in overnight sleep studies in a sleep lab. The Polysomnography (PSG) itself is a non-invasive, painless test but may be uncomfortable. Complications are rare. The most common side effects are as follows:

- Being unable to sleep in the sleep lab causing tiredness or fatigue the next day and loss of productivity
- Local irritation or bleeding of the skin where external electrode sites are attached
- Bruising, bleeding or soreness from external electrode removal

Risks associated with Drug-Induced Sleep Endoscopies (DISE)

You are required to undergo DISE procedures as part of this clinical trial. Administration of sedative medication (Midazolam and/or Propofol) in DISE is known to induce muscle relaxation which is an intended effect of this drug in this study. You may experience general fatigue, somnolence or even start sleeping after the injection, which is normal and somewhat expected.

The dose for the DISE procedure will be rather low compared to doses usually administered to participants receiving these drugs (Midazolam and/or Propofol) in the frame of their normal medical care.

Therefore, side effects rarely observed with these drugs at higher doses or after repeated administration are quite unlikely to be seen in this study. These known side effects are:

- Bradycardia (your heart beats more slowly)
- Visual disturbances
- Dry mouth
- Gastrointestinal disturbances
- Headaches, confusion
- Paradoxical reactions (e.g. aggressive behavior, hostility, hallucinations, disinhibition, excitation, irritability and increased anxiety)
- Slowing down your breathing (respiratory depression)

Some side effects may be severe if you suffer from liver impairment, respiratory problems other than OSA or if you have a known hyper sensibility to benzodiazepines, which is why the doctor will not enroll you in the study if you meet one of these conditions.

Intravenous injection can also cause local irritation of the skin at the injection site, which can result in red and itchy areas of the skin.

If you are allergic to egg products, soy, or glycerol please discuss this with your doctor. Propofol used in DISE contains egg lecithin, soybean oil, and glycerol, and the risk of allergy is particularly high if you are allergic to these.

Other side effects associated with DISE include the following:

- Nose bleeding
- Trauma to the upper airway
- Suspension of breathing episode
- Light-headedness
- Pain or irritation in the throat or nasal passage

Risks associated with pregnancy

The general anesthesia performed for the implantation surgery may present risks for the embryo if you are pregnant. In addition, the effects of the Genio® System 2.1 on the unborn child and on the new-born are not known. 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 remain OFF until you stop breastfeeding.

Storage and Handling

Storage Temperature

External system components should be stored in a clean area with room temperature of approximately +15 °C to +27 °C / +59 °F to +81 °F.

Do NOT expose the products to direct sunlight.

Humidity

Keep your Genio® external devices away from extremely humid areas and sources of water.

Expiration Date

Disposables Patches should not be used after the expiration date. Expiration date is indicated on component's packaging labels.

Handling

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

- The Activation Chip metal pins at the bottom of the chip should not be in contact with any surface except for the Disposable Patch, the Charging Unit docking area or the Activation Chip protection cover.
- The devices should not be placed on any metallic surfaces.

- We recommend that you leave the Activation Chip in the Charging Unit all day to ensure 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 adherence properties of the patches.

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
- Do not fold the Disposable Patches before use
- Disconnect the Charging Unit from its adapter

Wireless communication

Communication Interference between the smartphone and the activation chip may be temporarily disturbed 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.

This device complies with part 15 of the FCC Rules (FCC ID: 2A6HG-NX-ASM-002325). 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

3 Your Genio® System 2.1

Therapy Overview

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

If your doctor determines this therapy is suitable for you, the Implantable Stimulator will be implanted under your chin during a short surgical procedure. After a healing period of approximately 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 approximately 4 months. During this optimization period, you will have clinic visits and overnight sleep studies. Your doctor will determine when sleep studies are needed.

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

Patient Kit Contents

The enclosed Patient Kit contains the following components:

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

The Genio® System 2.1 Components

The Genio® System 2.1 components, namely the Implantable Stimulator, the Activation Chip, the Disposable Patch and the Charging Unit are described in the following.

Implantable Stimulator

The Implantable Stimulator is a small saddle-shaped looking 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 2 metal pads each, called electrodes. This implant is 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 normal breath while sleeping.

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 physician. The Activation Chip should be kept in the provided protective cover when it is not in use or not being charged.

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.

Disposable Patch

The Disposable Patch is a single-use adhesive patch made of an adhesive layer that is placed on the skin under the chin. The Disposable Patch has a clip to which the Activation Chip is snapped onto to connect them together. They will provide the external unit needed to transmit stimulation energy to the Implantable Stimulator.

Installing Your Genio® System 2.1

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

Battery Precautions: (1) Use **Only** the supplied Nyxoah charger and its power adapter. Any other power supply may damage the devices. (2) Do NOT use/store the devices nearby heating sources or under the blazing sun. (3) Do NOT open device housing.

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

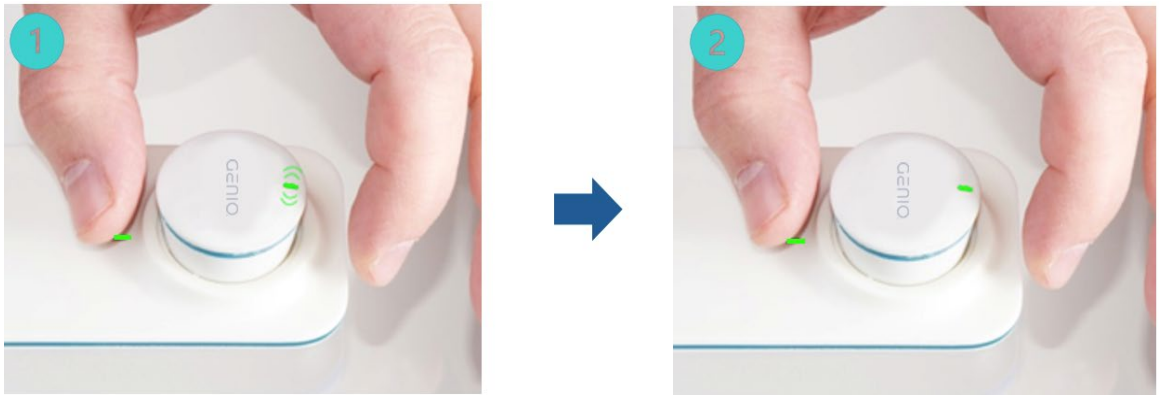
Do NOT touch the metal pins on the bottom of the Activation Chip and do NOT place these metal pins on any surface.

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

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 green light will start blinking on the Activation Chip, indicating charging.

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



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 6 “Visual Indications”.

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

Using Your Genio® System

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.

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.
Please also note that the Disposable Patches should not be used after the expiration date marked on the package.

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 - Ensure the Activation Chip is fully charged by verifying the green light on the Activation Chip is constantly on and gently take out the fully charged Activation Chip from the Charging Unit in order to reset it.

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.

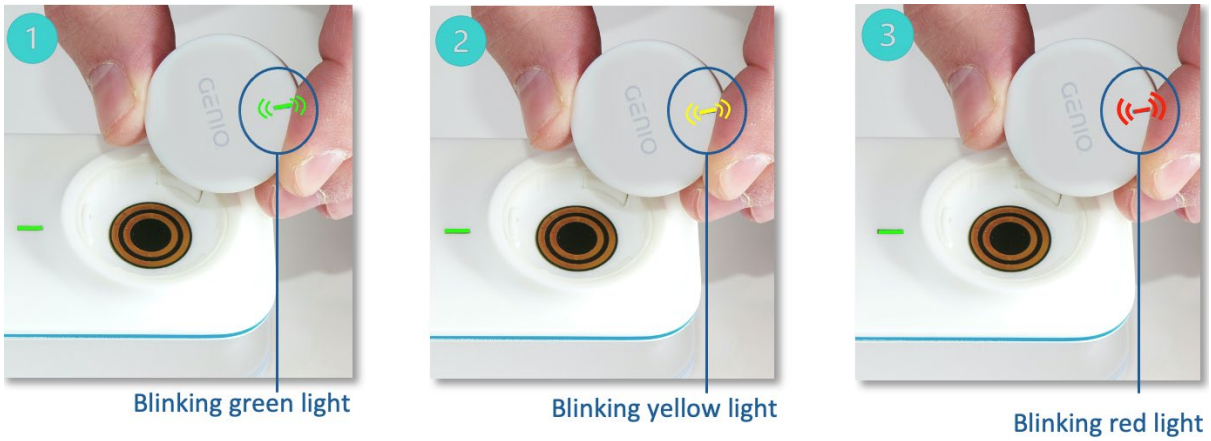
Upon removal from the Charging Unit, the Activation Chip light will blink in red, yellow and green once, indicating that it has been reset and is ready to be used.

Step 3 - The Activation Chip light will then start blinking as follows 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 battery of the Activation Chip is low and needs to be re-charged before being used for an entire night.

(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 before the chip is replaced. If this occurs, please contact your doctor as soon as possible.



Step 4 - With the Activation Chip light still blinking, 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.

The Activation Chip light will turn on as follows for a few seconds, indicating that it is properly connected to the Disposable Patch:

(1) If the steady light on the Activation Chip is green, 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, it means the Activation Chip battery is low and needs to be re-charged to ensure the battery will be sufficient for an entire night of use.

Note: A summary of the light indications of the devices is available in Section 6 “Visual Indications”.

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

The connection between the Activation Chip and the Disposable Patch must be performed while the light on the Activation Chip is blinking, otherwise, it should be reset again according to step 2.

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

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.

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.

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

Do NOT apply the Disposable Patch on breached or wounded 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 - Reposition your head in 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.

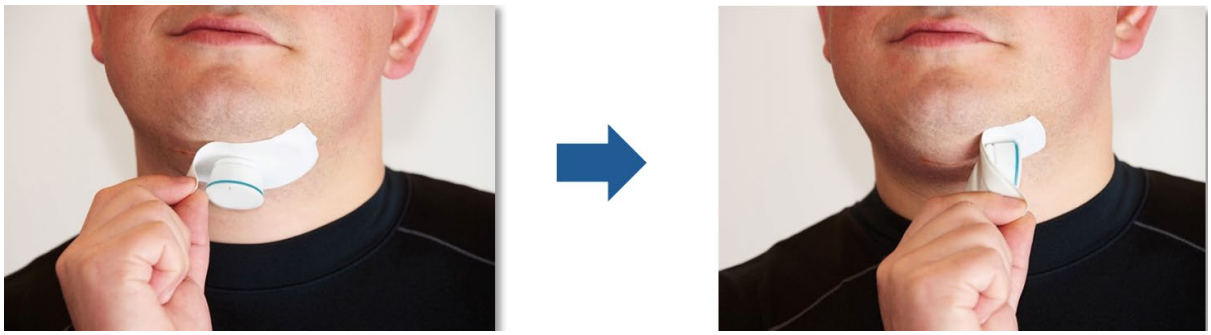
The system is now activated. You can go to sleep and enjoy a restful night. The stimulation will start automatically after the delay time set by your doctor. The delay time is a period during which no stimulation is delivered in order to allow you to fall asleep without feeling the stimulation.

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 in a direction as close as possible to the skin.

If you experience skin irritation where the patch was attached, please consult your doctor.



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

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 in compliance with local laws and regulations**.***

**If you are enrolled in a clinical investigational study (i.e. DREAM clinical investigation study), please remain compliant with returning used Disposable Patches as defined within the study plan.*

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

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.

The Activation Chip must be fully charged after each use.

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.

If the light does not turn on the Activation Chip light, 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 6 "Visual Indications".

4 Genio® Smartphone Application

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

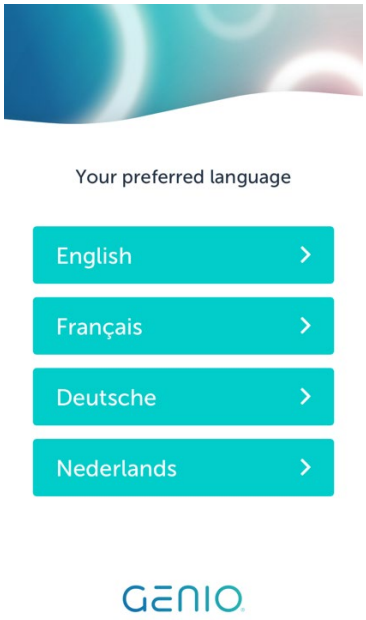
- Pause and resume treatment
- Adjust stimulation intensity within a range set by your sleep physician
- Access usage information

Installation

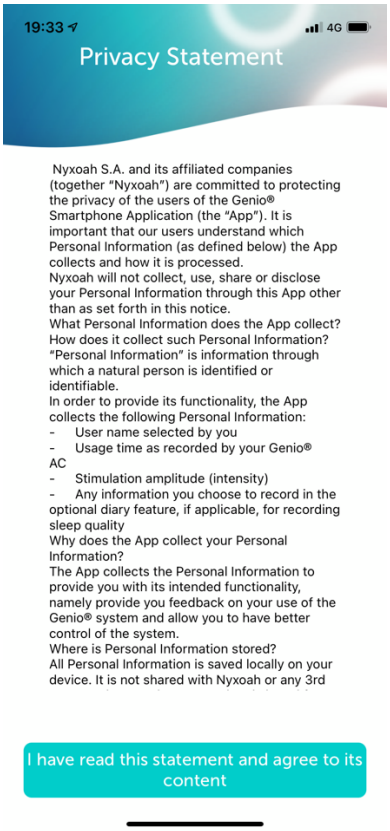
Application setup

To install and setup your Genio® Smartphone App, follow these steps:

1. Download and install the Genio® Smartphone Application from the App Store (on iPhones) or from Google Play (on Android devices).
2. Following successful installation, open the application on your smartphone. When prompted, confirm allowing the app using the smartphone's Bluetooth services. Disallowing the app to use the Bluetooth services will compromise the proper function of the app.
3. The application main screen will appear, followed by the language selection screen. Select your preferred language.

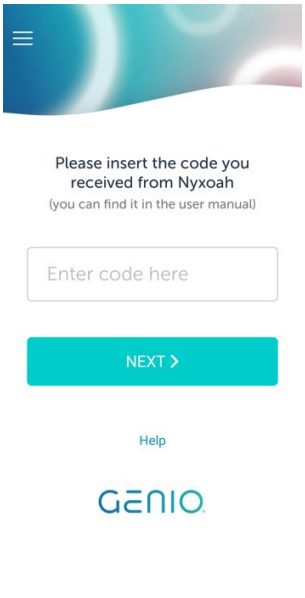


4. A Privacy statement will be displayed. Read the statement and confirm reading by pressing the consent button.

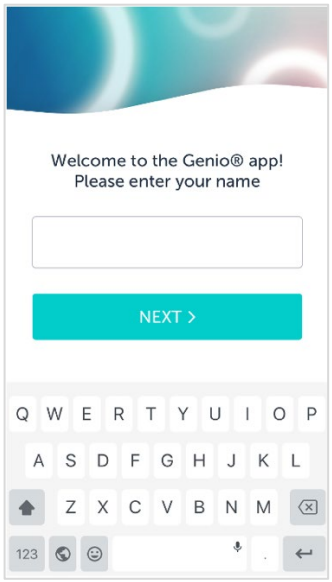


5. The Application authentication screen will appear. Enter the authentication code 5617 and press "Next".

If an incorrect code is entered, the authentication process will not be completed, and the application could not be used.



6. Finalize the app installation by entering your name and start using your Genio® Smartphone App.



7. A quick tour providing an overview of the Genio® Smartphone App screens will be displayed. Toggle between the tour screen by clicking next or swiping the screens to the left, click “Finish” to close the tour and start using the App. You can also close the tour by clicking the “Skip” button in the top right corner of the screen.

Activation Chip and App Pairing

To start using the application, your Activation Chip must be paired with your Smartphone App.

To pair your Activation Chip with your Smartphone App, follow the steps below:

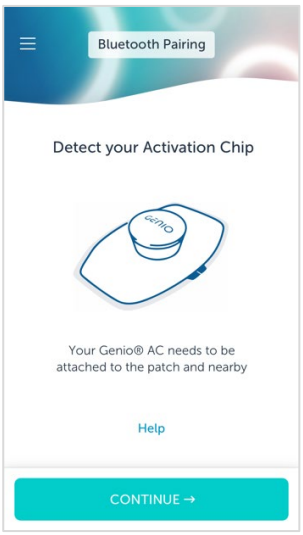
1. Take your Activation Chip out of the charger.
2. Identify the serial number of your Activation Chip. This number can be found on the label located at the bottom of the chip.

3. Place a Disposable Patch on a firm surface and connect the Activation Chip to the Disposable Patch. Ensure the light on your Activation Chip turns on upon DP connection, indicating they are properly connected.

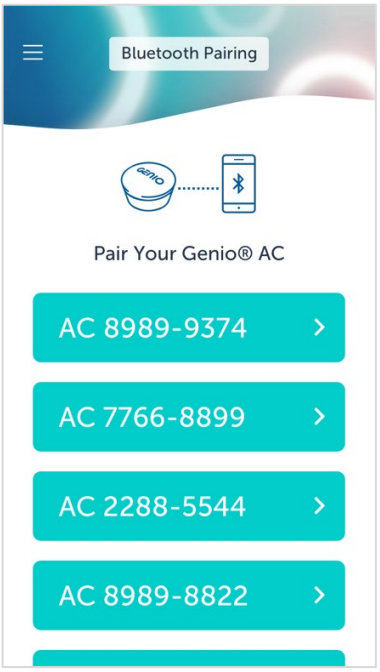
Do NOT place the DP on a metallic surface or near any type of metal. Attempting to attach the AC while the DP is close to metal may cause device malfunction.

Do NOT use excessive force when connecting the AC to the DP.

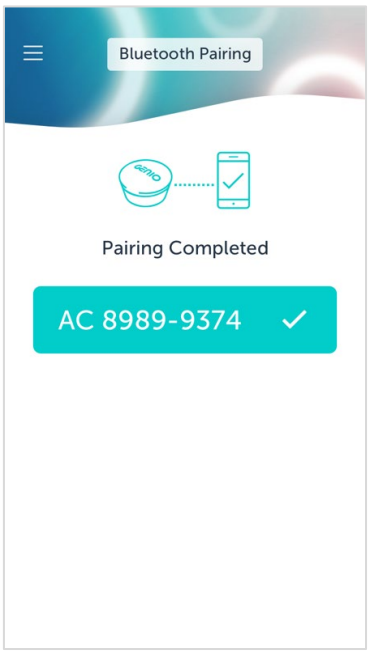
4. Open your Smartphone App.
5. When using your Smartphone App for the first time, the App will automatically offer you to look for Activation Chips nearby. While ensuring that your Activation Chip is connected to a Disposable Patch and is placed it next to your Smartphone, press “Continue”.



6. The application will display a list of all the Activation Chips detected. If there is more than one Activation Chip in the list, select the one that matches with the serial number written down underneath your Activation Chip.



7. When prompted by the application, insert the pairing key 123456 and confirm the pairing request. When prompted, confirm remembering the AC by the app. Failing to do so will lead to communication issues between the app and the AC in the next time the app is launched.
8. The application will indicate successful pairing when completed.
   Note: If the pairing of your Activation Chip failed, please refer to the Troubleshooting section (see section 5).



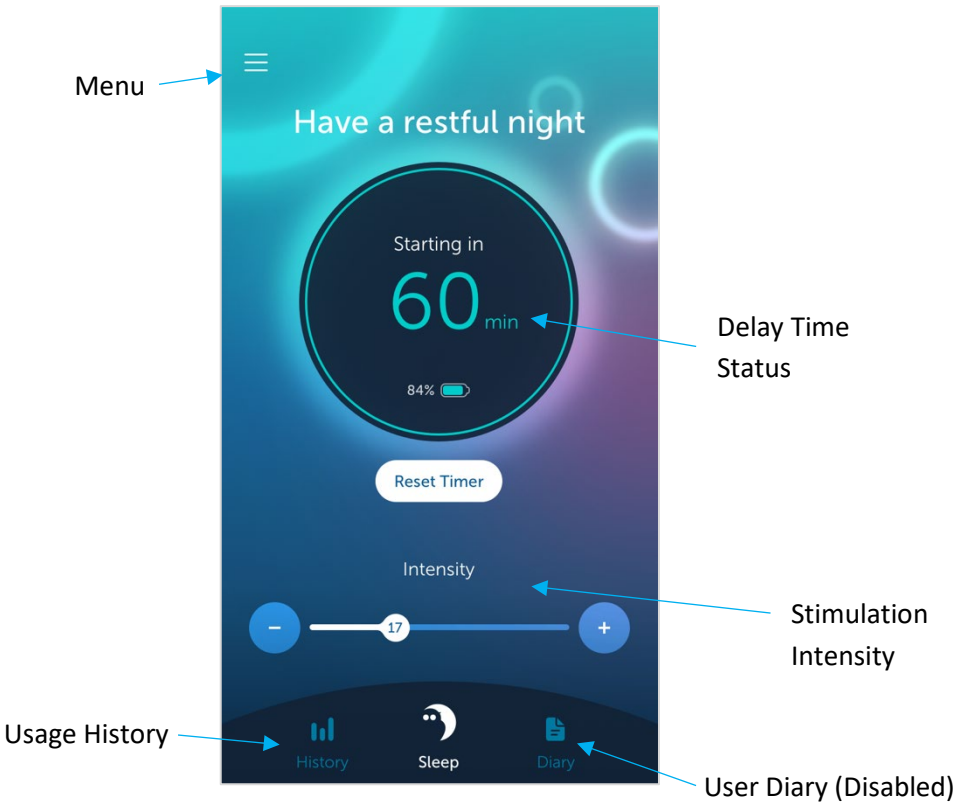
Congratulations, your Chip is now paired with your Smartphone Application!

Daily Use

On a daily basis, the Genio® Smartphone App will allow you to (see picture below):

1. Control your Genio® therapy, i.e., pause/resume stimulation, adjust the stimulation intensity and reset the delay time to its pre-set value.
2. Access usage history data.
   Note: The Diary feature is disabled for participants in the clinical study

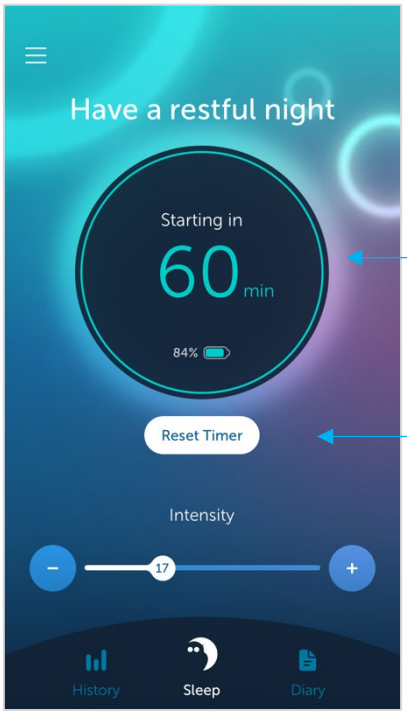
These features are detailed in the following sections.



Control your Genio® Therapy

Once your Genio® system 2.1 properly setup according to section 3, the Genio® Smartphone App allows you to control your therapy on three different levels:

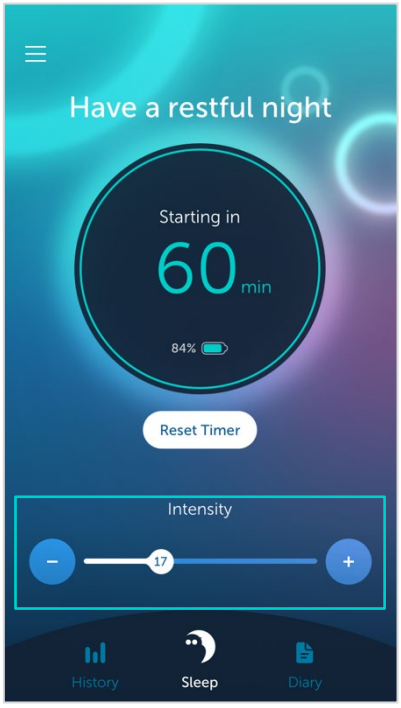
1. **Delay time:** Upon connection to a Disposable Patch, the countdown of your predefined delay time starts, after which the stimulation will be activated. The remaining time will be displayed on your Genio® Smartphone App. If you need more time and want to reset your delay time, press on “Reset timer”.



Delay time status

Reset delay time

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.



Adjustment of the stimulation intensity

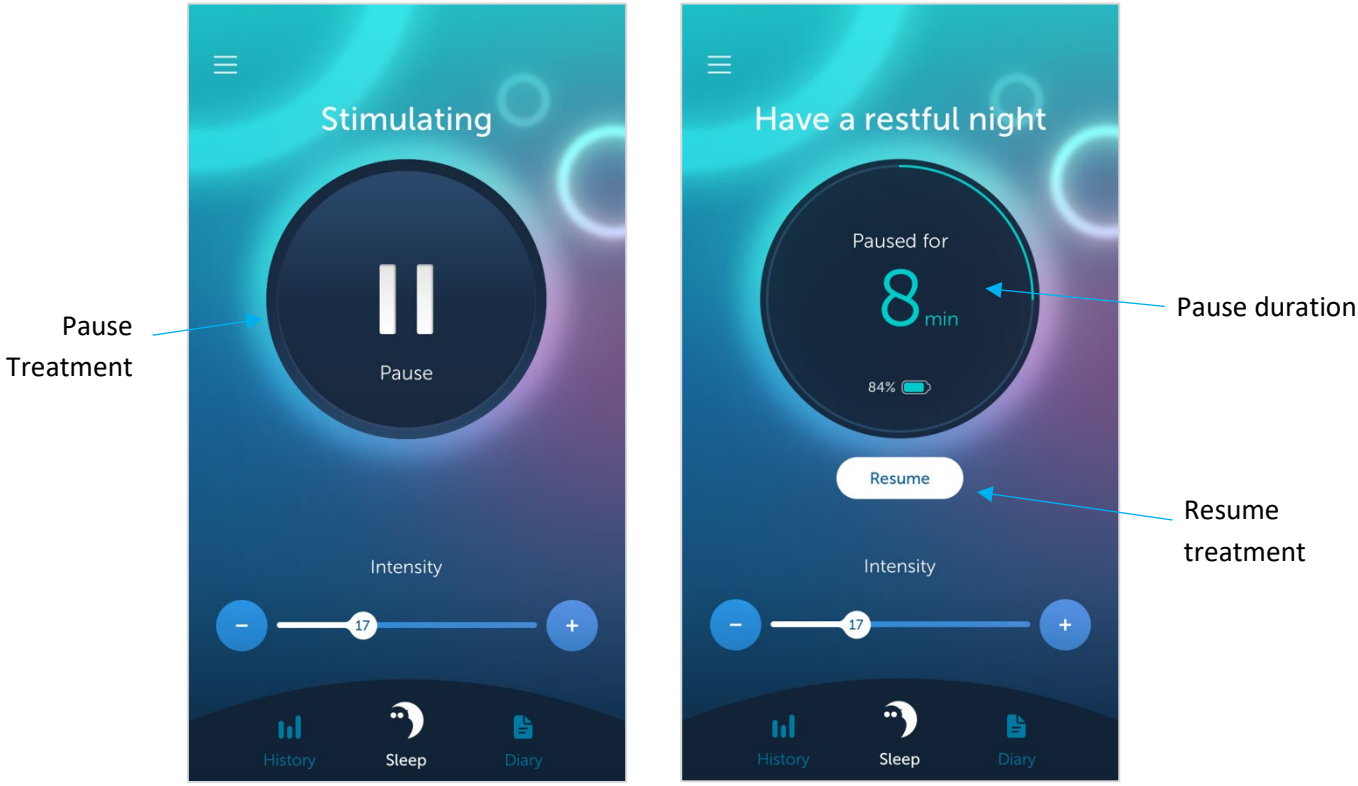
Adjusting the stimulation intensity can be done at any time:

- 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.

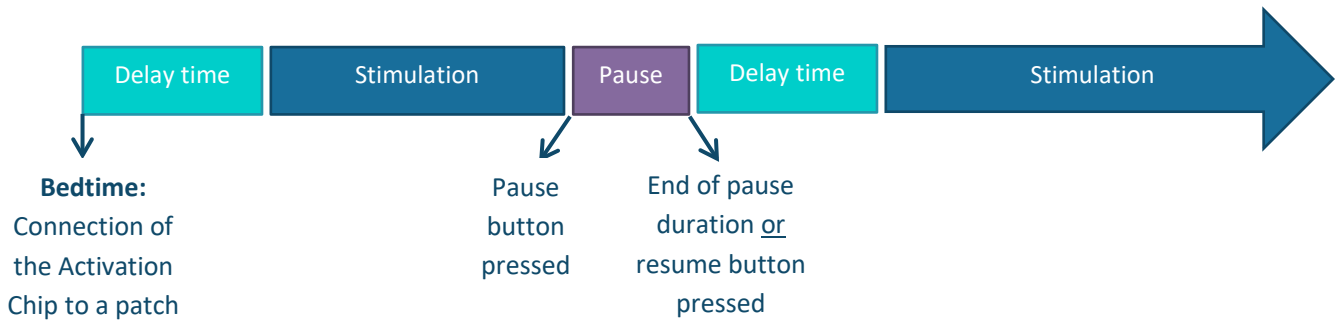
- If the intensity is changed <u>while the stimulation is on</u>, the change in intensity will be implemented for the next stimulation period (typically a few seconds later).

When updating the stimulation intensity, the selected intensity will be updated on the screen.

3. **Pause/Resume:** At the end of the delay time, the stimulation will start. You can pause stimulation for a predefined duration and resume treatment by pressing the "Pause" (see Figure below) and "Resume" buttons, respectively (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 App settings (see "Settings" section below).



To resume treatment, you can either press "Resume" 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 and your activation chip, make sure your activation chip is not in proximity to large metallic surfaces or other Bluetooth devices and retry using the application.

History Screen

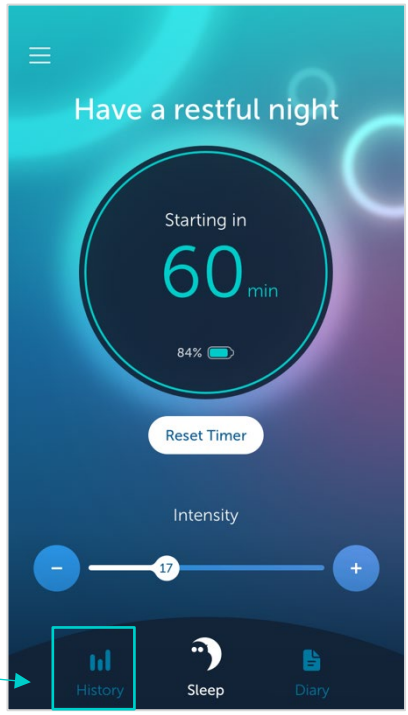
The Genio® Smartphone application provides information regarding the daily usage of your Genio® System 2.1.

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 app 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.

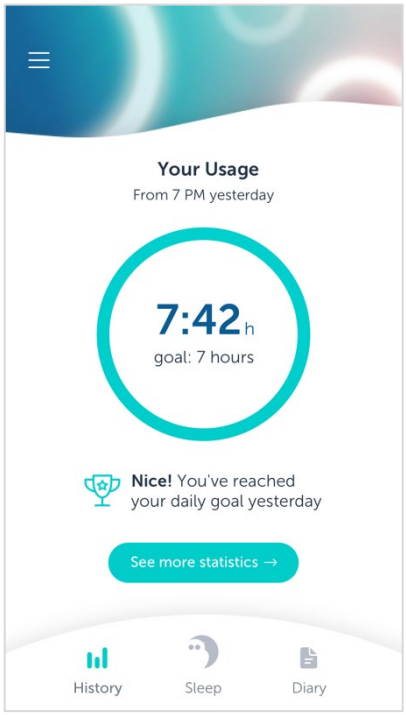
Note: The Activation Chip will store that log record for the last night only after it is reset by placing in the Charging Unit. If you wish the history view to include the last use period, make sure that the Activation Chip is reset before reconnected to a Disposable Patch and to the Smartphone App.

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 App was launched, if the Activation Chip is during the Delay period, the Delay timer will reset.

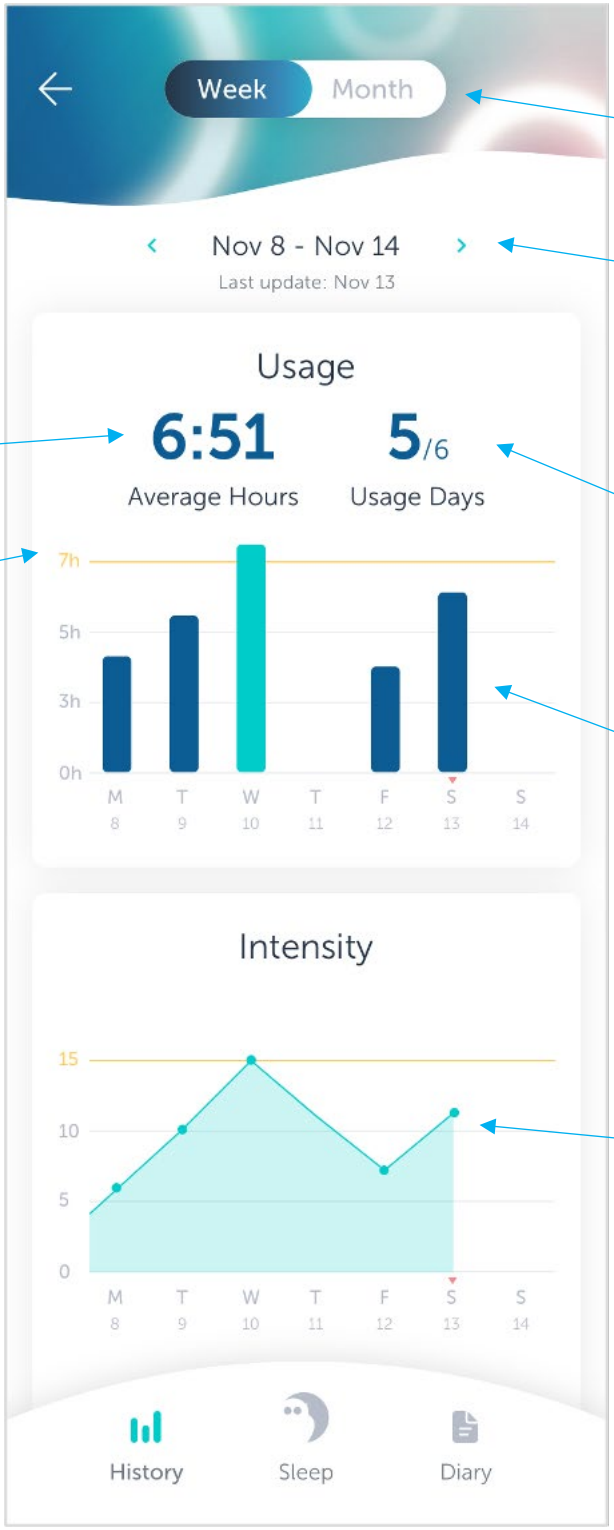


Usage History



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 7 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 diary.



Weekly/Monthly usage data

Selected week

Average number of hours the Genio system was used per night

Number of days the Genio system was used during analyzed period

Target usage duration

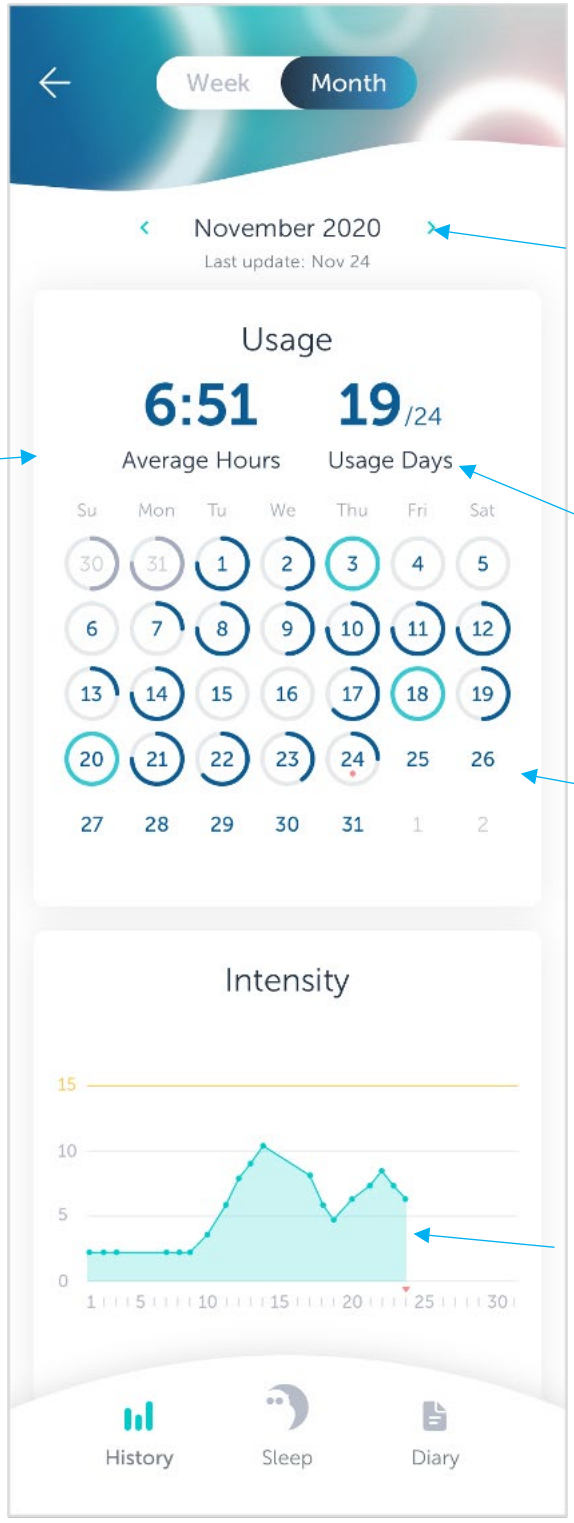
Number of hours used per night

Stimulation intensity used each night

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 7 hours.
- The stimulation intensity set each night during the selected timeframe.



Selected month

Average number of hours used per night

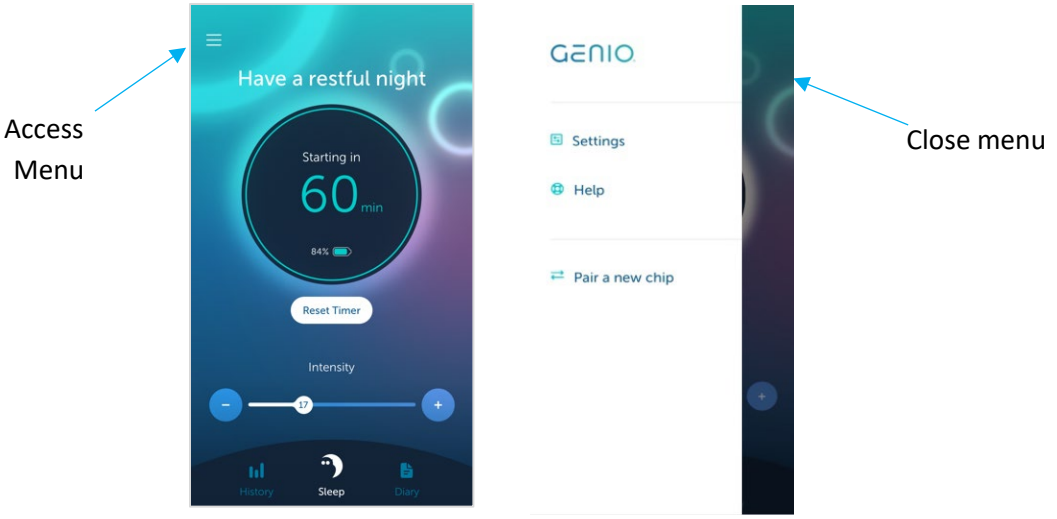
Number of days used

Number of hours used per night

Treatment amplitude per night

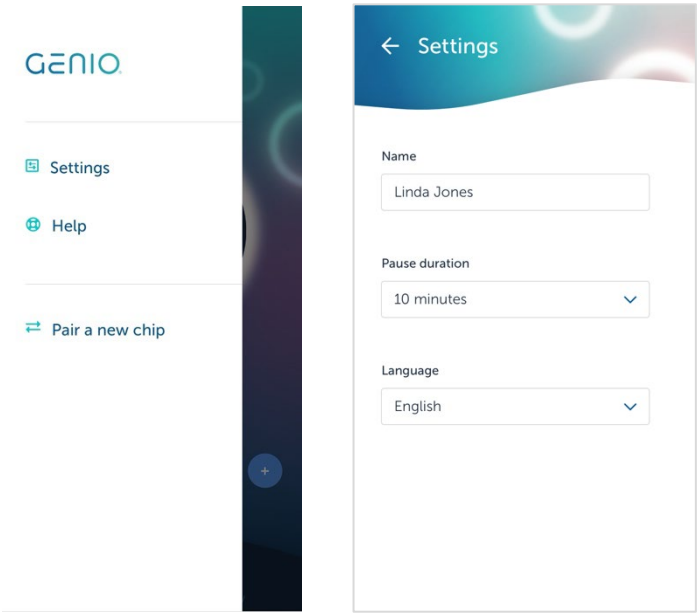
App Menu

The Smartphone App main menu can be accessed by clicking on the “Menu” symbol and enables access the following 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 App, click on the “Menu” symbol.



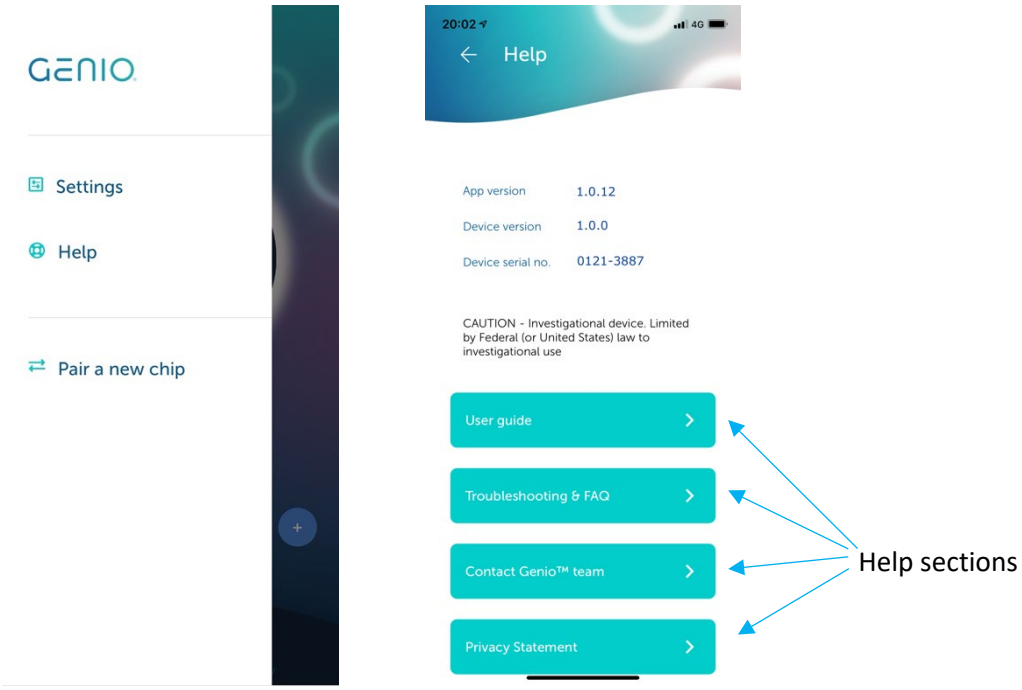
Settings

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



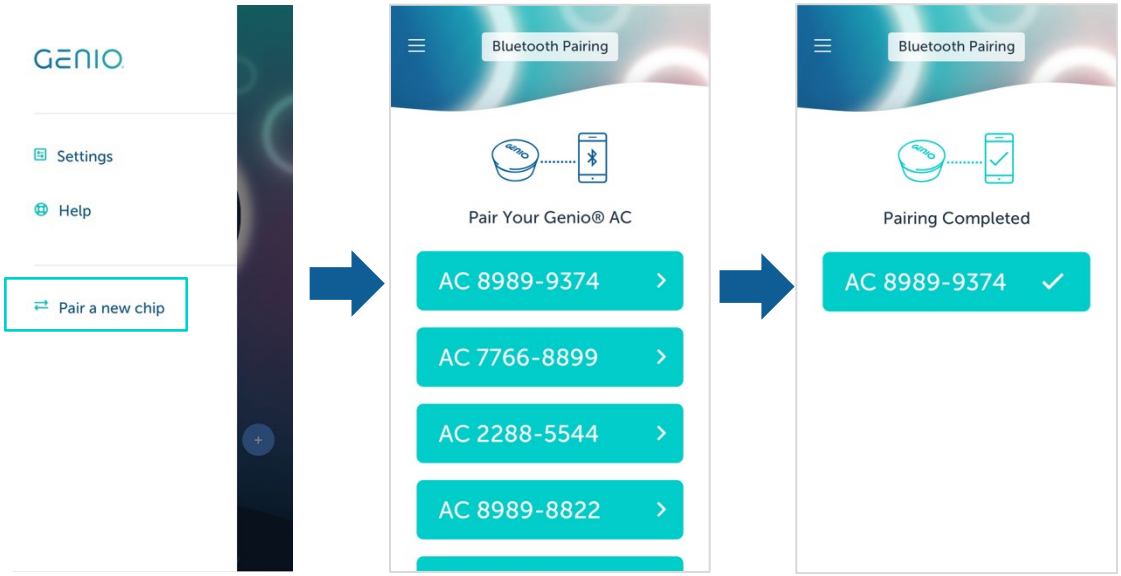
Help

The Help tab includes device information such as the Smartphone App version, the Activation Chip version and serial number, as well as some help sections. i.e., the user guide, a troubleshooting section, a FAQ section and a contact form.



Pairing a new Activation Chip

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



5 Troubleshooting

This section details troubleshooting for the Genio® System 2.1. If your question or problem is not addressed in the following, contact your doctor.

Note: A summary of the light indications of the devices is available in Section 6 "Visual Indications".

General Troubleshooting for the Genio® System 2.1

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.

The tongue stimulation began before I fell asleep

If you feel that your tongue is being stimulated before you fall asleep, consult your doctor. 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.

I felt discomfort when using the Genio® System 2.1

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

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.

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 store the used patch in a re-sealable zipper storage bag provided in the Patient Kit and bring it to your doctor at your next visit.

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.

Do not forget to put both used Disposable Patches in the re-sealable zipper storage bag the next morning and to tell the doctor that you used two Disposable Patches that night.

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 doctor at the earliest opportunity.

Troubleshooting Specific to the Activation Chip

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, report this to your doctor at the earliest opportunity.

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 doctor at the earliest opportunity in order to get a new Activation Chip.

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.

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. If not, repeat steps 2 and 3.

The Activation Chip was dropped or suffered damage

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

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 doctor at the earliest opportunity.

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.

Troubleshooting Specific to the Charging Unit

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.

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.

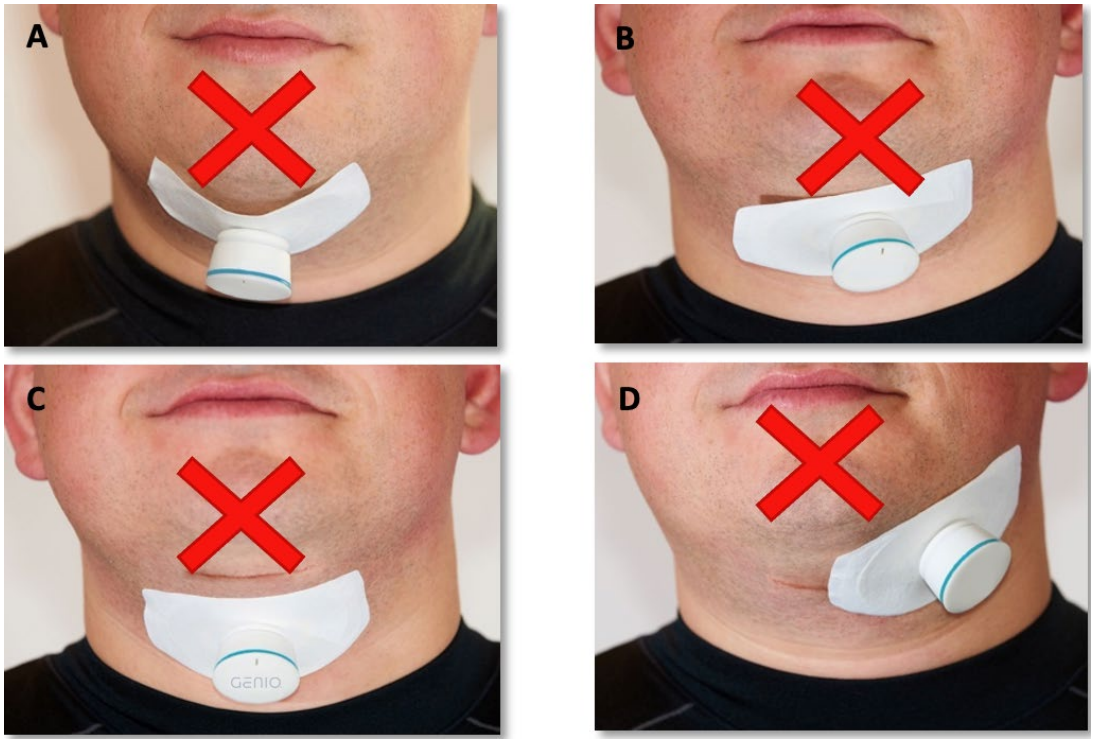
Step 2 - Verify that the power adapter cable is properly connected to the Charging Unit.

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

Troubleshooting Specific to the Disposable Patch

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.



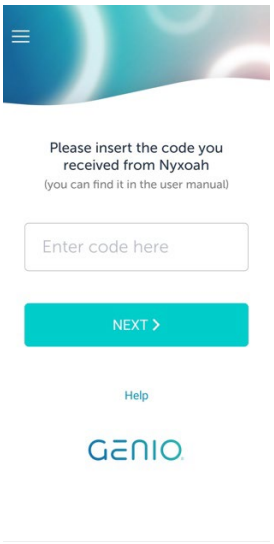
Incorrect positions of the Disposable Patch. (A) Center of the Disposable Patch not fully attached to the skin. (B) Border of the Disposable Patch not fully attached to the skin. (C) Disposable Patch positioned too low (on the neck). (D) Disposable Patch not aligned with the center of chin.

Troubleshooting specific to the Genio® Smartphone App

I entered a wrong authentication code

If the authentication code is incorrect, ensure you entered the correct code. Your authentication code is provided in this manual to complete installation.

If you have inserted the provided code and the problem persists, remove the application from your smartphone, re-install it and type-in the authentication code as instructed. If the problem persists, contact Nyxoah.



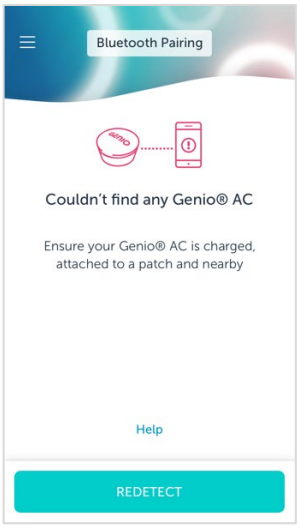
The Smartphone App did not find my Activation Chip when attempting to pair them

If the following screen is presented on your smartphone when attempting to pair your App with it, it means your Activation Chip may not be sufficiently charged or is not properly connected to a Disposable Patch.

Before initiating the pairing process, make sure that your chip:

- Is fully charged,
- Has been properly reset in the Charger,
- Is connected to a patch, and
- Is located nearby your smartphone.

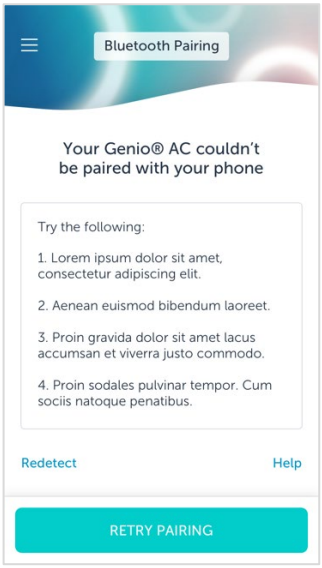
Press “Redetect” to launch another search of your chip. If your Activation Chip can still not be found by the application, contact Nyxoah.



I could see my Activation Chip in the pairing list but could not complete the pairing process

If you could see your Activation Chip serial number in the pairing list but your Activation Chip could not be paired with your Smartphone App, follow these steps:

1. Make sure that the correct Activation Chip was selected for the pairing process.
2. Verify that the Activation Chip serial number printed on the product label underneath your Activation Chip is identical to the number displayed by the Smartphone App.
3. If the number is not identical, press “Redetect” and look for your Activation Chip in the list of Activation Chips found by the application.
4. Select your Activation Chip and pair it with the application, insert the pairing code provided in this manual and confirm remembering the device by the application.
5. If pairing failed, refer to the previous troubleshooting section.
6. If problem persists, contact Nyxoah.



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 AC 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 problem persists, contact Nyxoah.

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.

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 App.
2. If your Activation Chip is not detected by the Smartphone App, 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 App.
3. If you have reached the maximal intensity available and the problem persists, contact Nyxoah.

Wireless communication

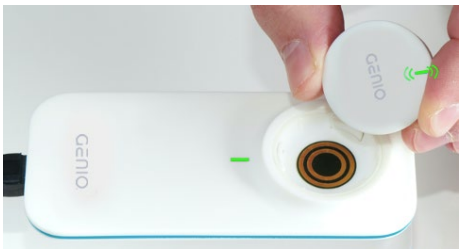
Communication Interference between the smartphone and the activation chip may be caused temporarily by other wireless devices or proximity of your activation chip to large metallic surfaces. To reduce or stop interference, move away from the source. The effect is temporary and will not damage your device.

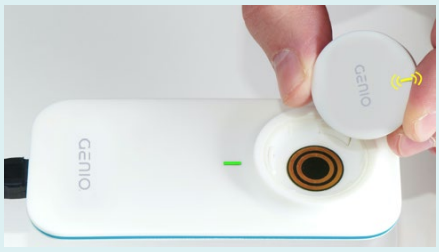
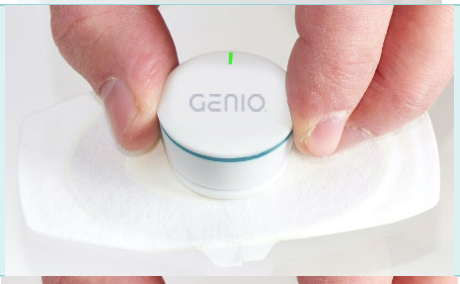
If you experience wireless communication issues between your Smartphone app and your Activation Chip:

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 in proximity to your Smartphone
4. Verify that the Activation Chip and Disposable Patch are not located in proximity to large metallic surfaces

In case you are unable to pause stimulation using the Smartphone App, remove the AC from the DP to stop stimulation immediately.

6 Visual Indications

Light indication	Action	Picture
Steady green light on power adapter	The power adapter is properly connected to power	
Steady green light on Charging Unit	The Charging Unit properly is 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 removed from the Charging Unit)	The Activation Chip is fully charged and ready to be connected to a Disposable Patch	

Light indication	Action	Picture
Blinking yellow light on Activation Chip (after removed from the Charging Unit)	The Activation Chip is not fully charged and can be connected to a Disposable Patch	
Blinking red light on Activation Chip (after removed 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 and is not fully charged	

7 Cybersecurity

- The Genio® System is designed to reduce cyber-security threats and minimize the system's vulnerability to cyber security attacks.
- Communication between your AC and Smartphone application is based on Bluetooth Low Energy (BLE) and requires pairing and bonding of the devices before use. Communication is protected by data encryption (AES 128) to reduce cyber security related threats.
- Communication between the Smartphone App and AC requires the devices to be in proximity of each other, and AC cannot be controlled remotely.
- No sensitive data is stored on any component of the Genio System, including the Smartphone application.
- Never try to connect the device with cellular application other than Nyxoah certified application from the App store or Google play.
- Before installing the software verify that official 'Genio' appears under the application name.
- The Smartphone application is designed to operate on the following Operating Systems:
    - iOS versions 13 and above
    - Android versions 10 and above.
- In order to reduce cyber-security threats during use of the system, it is recommended to follow the guidelines listed below:
    - The Remote-Control Smartphone Application enables controlling the stimulation intensity of the AC. Consider adding a password protection for your Smartphone in order to prevent unauthorized stimulation intensity changes which may result in temporary discomfort.
    - Smartphone application installation is password protected. Make sure to install only a certified App version via the Apple AppStore or Google Play Store.
- Please contact Nyxoah in case that cybersecurity is compromised/ or suspected to be compromised in your product.

8 Operational Specifications

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 doctor.**

Keep away from children.
All devices must be used at a temperature between +15 °C and +27 °C / 59 °F to 81 °F.

9 Symbols on Product or Package Labeling

Catalogue Number

Serial Number

Use by Date

Lot Number

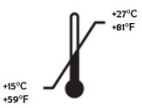
Date of Manufacture

Do not re-use

Store in a cool place away from direct sunlight

Manufacturer information

Store in a dry place



Temperature Limit (according to storage specifications)

Do not use if package is open or damaged

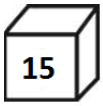
Caution/Important information

RF Symbol; Non-Ionizing Radiation

Consult Instructions for Use

Waste Electrical and Electronic Equipment Directive

Double Insulation



Quantity per Box

Transport Relative Humidity Range

IPX

IP Classification

Type BF Applied Parts

MR Conditional

UDI (Unique Device Identification) information

Federal Communications Commissions

10 EMC Requirements

Use Environment

The Genio® System 2.1 (AC, DP, IS, CU, Power Adapter, ES parts) is intended for use in professional healthcare facility environment (such as Operating Room, Sleep Lab, Physician offices and clinics and hospitals, except medical treatment areas with high-powered RF equipment).

The Genio® System 2.1 (AC, DP, IS, Power Adapter and CU parts) is intended for use in home healthcare environment.

Essential Performance

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

Device	Essential performance functions
IS	Delivering stimulation pulses according to 8 MHz electromagnetic field transmitted from an external device (AC or ES)
AC and DP	Transmission of modulated 8 MHz EM field to power the IS
AC	Activation and handling of BLE interface Charging AC battery
ES	Transmission of modulated 8 MHz EM field to power the IS
CU and Power Adapter	Charging AC battery

Wireless functions

System component	Specific RF wireless type	Type	Wireless functions
IS	Wireless modulated energy transfer 8 MHz	Receiver	Receiving stimulation energy and pattern from ES or AC-DP
AC-DP	Wireless modulated energy transfer 8 MHz	Transmitter	Energy transfer to IS
	BLE (Bluetooth Low Energy) 2.4 GHz	Transceiver	Communication and data transfer between Genio® AC and Smartphone application software
Patient smartphone	BLE (Bluetooth Low Energy) 2.4 GHz	Transceiver	Communication and data transfer between Genio® AC and Smartphone application software

Genio® application			

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 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.

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
AC+DP	4.2 V, 160 mAh (Battery Powered)	8 MHz BLE: 2.4 GHz
ES	3.7 V, 120 mAh (Battery Powered)	8 MHz
CU	110-240 V, AC 50-60 Hz	N/A

EMC Guidance Tables

Guidance and manufacturer's declaration – electromagnetic emissions IEC 60601-1-2 Ed.4

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	

Guidance and manufacturer's declaration – Electromagnetic Immunity IEC 60601-1-2 Ed.4

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.
NOTE: U_T is the AC mains voltage prior to application of the test level.			

Guidance and manufacturer's declaration – electromagnetic IMMUNITY IEC 60601-1-2 Ed.4

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	

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 (ES)	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 (AC-DP)	Tx	8 [7.985-8.01125]	7.4-8.8	Per Treatment Protocol	H-Field strength: 34.7 dB (µA/m) (54.3 µA/m)