Altius® Direct Electrical Nerve Stimulation System
Prescriber Instructions for Use

Caution: Federal (US) law restricts this device to sale by or on the order of a physician.
LB-0195 Rev B

ALTIUS SYSTEM PRESCRIBER INSTRUCTIONS FOR USE

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The information provided in this document may change without prior notice.

Please read the complete documentation provided before you use the device.

Although FDA has determined that the probable benefits outweigh the probable risks, there remains some uncertainty regarding the manufacturer's human factors engineering (HFE) and usability engineering (UE) analysis and validation testing. As a condition of approval, FDA is requiring the manufacturer to provide an HFE/UE analysis and validation testing and recommending that this analysis and testing is designed using the FDA's 2016 guidance document "Applying Human Factors and Usability Engineering to Medical Devices" (https://www.fda.gov/media/80481/download).

This manual can also be found at: www.neurosmedical.com

The Altius® System is protected by several U.S. Patents.

For an up-to date list of relevant patents and patent applications, visit our patents page:
https://www.neurosmedical.com/patents

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Information available for the Altius System:

The information for prescriber manual provides information about indications, contraindications, warnings, precautions, adverse events, sterilization, patient selection, individualization of treatment, and component disposal.

Product manuals, such as programming guide, patient user guide, and implant manual provide device descriptions, package contents, device specifications, battery longevity and instructions for use.

For information that supports the clinical use of the Altius System, refer to the clinical summaries manual.

ALTIUS SYSTEM PRESCRIBER INSTRUCTIONS FOR USE

1. Indications for Use, Contraindications, Warnings and Precautions

1.1. Indications for Use

The Altius® Direct Electrical Nerve Stimulation System is indicated as an aid in the management of chronic intractable phantom and residual lower limb post-amputation pain in adult amputees.

1.2. Contraindications

The Altius System is contraindicated for patients who are:

- Unable to operate the system.
- Unsuitable for the Altius implant surgery

1.3. Operating Principle

The Altius System for Direct Electrical Nerve Stimulation is intended for the treatment of chronic intractable phantom and residual lower limb post-amputation pain. The system uses direct electrode-to-nerve contact via a nerve cuff electrode to directly administer electric stimulation on the nerve terminus of the amputated lower extremity to alleviate pain. Neuros Medical's unique Direct Electrical Nerve Stimulation technology holds the promise of providing an effective, mechanism-based yet non-destructive, treatment for managing chronic intractable phantom and residual lower limb post-amputation pain in adult amputees. This technology was developed based on the findings from pre-clinical animal experiments that continuous application of high frequency alternating current (HFAC), with a relatively high amplitude, could result in a sustainable yet reversible electrical conduction block in a nerve. [1,2] Both computer simulation and animal experiments have shown this electrical block is local, predictable, sustainable, and reversible. The Altius System is intended to generate a HFAC electrical stimulus similar to the one used in the animal experiments.

While conventional nerve block by injection of local anesthetic, such as lidocaine, can often provide predictable and reliable relief of pain of peripheral origin, the short-lasting effect and the toxicity of these agents have prevented their long-term use.

The clinical benefit of Direct Electrical Nerve Stimulation technology results from its direct action on pain signals without toxicity. Specifically, the HFAC waveform may inactivate the target nerve and consequently block pain signal transmission. We hypothesize that this electrical conduction block is achieved through the inactivation of sodium channels by sustained depolarization of the cell membrane.

1.4. Warnings

1.4.1. Use as indicated and instructed

Only use compatible products for the indicated therapy and indicated populations. Failure to use compatible products per labeling indications and instructions may result in product damage, patient injury, or death.

[1] Kilgore, K.L. and Bhadra, N. (2004) Nerve conduction block utilizing high-frequency alternating current. *Medical & Biological Engineering and Computing* ***42****, 394-406*.

[2] Bhadra, N. and Kilgore, K.L. (2005) High-frequency Electrical Conduction Block of Mammalian Peripheral Motor Nerve. *Muscle & Nerve* ***32****: 782-790*.

1.4.2. Diathermy

Diathermy should not be used on patients with the Altius System, or any of its components, either as a treatment for a medical condition or as part of a surgical procedure. The energy generated by diathermy can be transferred through the Altius System, possibly causing tissue injury, severe injury, or death. The Altius Implantable Pulse Generator (IPG), whether on or off, may be damaged. Refer to Appendix I: Electromagnetic interference for further information.

1.4.3. Electromagnetic Interference (EMI)

Electromagnetic interference (EMI) is a field of energy generated by equipment found in the home, work, medical, or public environments that is strong enough to interfere with Altius System function. Altius includes features that provide protection from EMI. However, sources of strong EMI can result in the following:

- Serious patient injury or death, resulting from heating of the implanted components of the Altius System and damage to surrounding tissue.
- System damage, resulting in a loss of or change in symptom control, and requiring surgical replacement.
- Operational changes to Altius, causing it to reset and turn off, which may result in decrease in treatment effect.
- Unexpected changes in stimulation, causing a momentary increase in stimulation or intermittent stimulation, which some patients have described as a jolting or shocking sensation. Although the unexpected change in stimulation may feel uncomfortable, it does not damage the device or injure the patient directly. In rare cases, as a result of the unexpected change in stimulation, patients have fallen down and been injured.

This note applies to the Programmer Wand of the Altius System:

NOTE: The EMISSIONS characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

Refer to

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Table **1**: Potential effects of EMI from equipment or procedures and Appendix I: Electromagnetic interference for information on sources of EMI, the effect of EMI on the patient and the neurostimulation system, and instructions on how to reduce the risk from EMI.

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Table 1: Potential effects of EMI from equipment or procedures

Equipment or procedure	Serious patient injury	Device damage	Device turns off/on	Momentary increase in stimulation	Intermittent stimulation
Diathermy	X	X	X	X	X
Magnetic resonance imaging (MRI)	X	X	X	X	X
Electrocautery	X	X		X	
RF nerve lesioning	X	X		X	X
Defibrillation cardioversion	X	X		X	X
Radiation therapy		X			
Lithotripsy		X			
Transcutaneous electrical nerve stimulation (TENS)			X	X	
Household items			X	X	
Theft detectors			X	X	X
Industrial machinery			X	X	X
Transmitting devices			X	X	X
Cellular and mobile phones			X	X	X

1.4.4. Case Damage

If the IPG case is ruptured or pierced due to outside forces, severe burns could result from exposure to the battery chemicals.

1.4.5. Packaging, Sterilization and Single Use

The Altius IPG, Cuff Electrodes, and kit contents were sterilized with ethylene oxide prior to shipment. Check the expiration date on the package before opening the sterile package and using the contents. Do not use the contents after the expiration date, if the sterile barrier is breached, or if contamination is suspected because of a defective sterile package seal.

- Do not use any component that shows signs of damage.
- Do not use if "Use Before" date has expired.
- Do not attempt to re-sterilize the contents of the sterile package that has been damaged or in any way compromised. Return any unopened devices to Neuros Medical.
- The Altius IPG, Cuff Electrode, port plug, are single-use only devices. Do not re-implant for any reason.
- An Altius System IPG that has been explanted for any reason may not be reimplanted in another patient.

1.4.6. Effects on other implanted devices

Altius interaction with implanted cardiac devices - When a patient's medical condition requires both a neurostimulator and an implanted cardiac device (eg, pacemaker, defibrillator), physicians involved with both devices (eg, anesthesiologist, neurosurgeon, cardiologist, cardiac surgeon) should discuss the possible interactions between the devices before surgery.

The electrical pulses from the Altius System may interact with the sensing operation from a cardiac device and could result in an inappropriate response of the cardiac device. To minimize or prevent the cardiac device from sensing the Altius System output:

- Implant the devices on opposite sides of the body
- Consider using bipolar sensing on the cardiac device
- Careful programming and review of each system's performance is necessary to ensure safe cardiac system operation with effective neurostimulation therapy.
- See also "Programmer interaction with other active implanted devices."
- Programmer interaction with other active implanted devices - When a patient has an Altius and another active implanted device (eg, pacemaker, defibrillator, neurostimulator), the radio-frequency (RF) signal used to program these devices may reset or reprogram the other device.

To verify that inadvertent programming did not occur, clinicians familiar with each device should check the programmed parameters of each device before the patient is discharged from the hospital, and after each programming session of either device (or as soon as possible after these times).

Also, inform patients to contact their physician immediately if they experience symptoms that could be related to either device, or to the medical condition treated by either device.

Patient control devices may affect other implanted devices - Patients should not place a patient control device (eg, controller, charger) over another active implanted medical device (eg, pacemaker, defibrillator, another neurostimulator). The patient control device could unintentionally change the operation of the other device.

1.4.7. Use in pediatric patients

Safety and Effectiveness of Altius System for pediatric use have not been established.

1.4.8. Use in pregnant patients

Safety and Effectiveness of Altius System for pregnant patient use has not been established.

1.4.9. Use in diabetic patients

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

- A preoperative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease, those with autonomic neuropathy or renal failure, and patients with a Hemoglobin A1C (HbA1c) ≥ 8% (64 mmol/mol).
- Monitor the patient's blood glucose levels in the perioperative period and instruct the patient to continue to monitor levels as they may fluctuate as a response to surgery or to complications. Implanting physicians and/or anesthesiologists should consult practice guidelines for the intraoperative management of diabetic patients during surgery.
- Closely monitor patient for signs of infection or delayed wound healing, as the severity of these complications may be greater in diabetic patients.

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1.5. Magnetic resonance imaging (MRI) Safety Information

Safety of MRI/NMRI with an implanted Altius System has not been evaluated. Patients implanted with the Altius System, or any of its components, should not be subject to MRI/NMRI. MRI exposure may result in dislodgement of the Altius IPG or Cuff Electrode(s), heating of the Altius IPG, injury to the nerve, and increased voltage through the Cuff Electrodes or Altius IPG. If MRI/NMRI is needed for any reason, the Altius System must be explanted prior to the diagnostic MRI/NMRI. For patients implanted with the Altius IPG, receiving an MRI/NMRI diagnostic scan, without first explanting the IPG may result in severe patient injury, death or device malfunction.

1.6. Precautions

1.6.1. Physician training

Implanting physicians. Implanting surgeons should be familiar with lower limb surgical procedures and should review the procedures described in the implant manual before surgery.

Prescribing physicians. Prescribing physicians should be experienced in the diagnosis and treatment of chronic post-amputation pain and should review prescriber information for Altius.

1.6.2. Storage and Operating Environments

The Altius IPG and the Cuff Electrode(s) are permanent implants, they are intended to be able to be used in the home and hospital and general environment while implanted in the patient. The Patient Controller and the Battery Charger are intended to be used in the home or general environment, while the programmer system, including the Programmer Wand is intended for use in the professional healthcare environment such as a hospital, clinic, or doctor's office.

Store the Altius IPG between -30° C and 60° C (-22° F and 140° F), and store the Cuff Electrode between -29° C and 60° C (-20° F and 140° F). Components of the Altius System should always be kept in temperature-regulated areas within the acceptable temperature range. The Altius IPG damage can occur at temperatures outside of this range. The IPG is designed to function between 17° C and 40° C (62.6° F and 104° F).

The Altius Battery Charger and Patient Controller is intended to be stored and transported between -25^{0}C and 70^{0}C (-13° F and 158° F).

The operational temperature range for use of the Battery Charger and Patient Controller is between 5^{0}C and 40^{0}C (41° F and 104° F). Relative Humidity range of 15% - 90%. Atmospheric Pressure of 700 hPA – 1060 hPA, or from 10,000 ft above sea level (Pressurization of a commercial aircraft) to 1,300 ft below sea level (the lowest elevation of dry land on earth)

The Altius Programmer Wand is designed to function normally after it has been exposed (While packaged for transport) to the following environmental extremes of -30° C and 60°

C (-22° F and 140° F), relative humidity between 20% and 75%; and atmospheric pressure between 500 hPa and 1060 hPa.

Recommended conditions for normal use of the Programmer wand is 10° C and 40° C (50° F and 104° F), relative humidity between 20% and 75%; and atmospheric pressure between 700 hPa and 1060 hPa.

The Altius PAPC is designed to function normally after it has been exposed (While packaged for transport) to the following environmental extremes of -20° C and 60° C (-4° F and 140° F), relative humidity between 20% and 75%; and atmospheric pressure between 500 hPa and 1060 hPa

Recommended conditions for normal use of the PAPC is 5° C and 35° C (41° F and 95° F), relative humidity between 20% and 75%; and atmospheric pressure between 700 hPa and 1060 hPa.

1.6.3. Component Handling

All system components and accessories should be handled with care. External devices should not be dropped, submerged in water, or operated in the rain. Avoid all sources of water that can come into contact with the external devices. Although reliability testing has been performed to ensure quality manufacturing and performance, dropping the devices on hard surfaces or in water, or other rough handling, can cause permanent damage.

1.6.4. Patient Detoxification

Before conducting lidocaine injection screening, patients should be detoxified from narcotics. If patients are not detoxified, screening may not be properly assessed.

1.6.5. Effect on electrocardiograms (ECGs)

Ensure the IPG is not delivering therapy prior to initiating an ECG. If the IPG is delivering therapy during an ECG, the ECG recording may be adversely affected, resulting in inaccurate ECG results. Inaccurate ECG results may lead to inappropriate treatment of the patient.

Refer to "Appendix I: Electromagnetic interference" on page 16 for information about other medical procedures that may interact with the Altius System.

1.6.6. Charging system

Wound contact. DO NOT use the recharger on an unhealed wound. The charging system is not sterile and contact with the wound may cause an infection. Patients should have gauze and/or clothing between the charger to avoid direct contact with the wound or skin.

Recharger use. Check for skin irritation or redness near the Altius IPG during charging. Do not lie on the IPG or apply excessive pressure to the IPG during charging. Take periodic breaks during prolonged charging.

1.6.7. Information for the patient

Activities requiring excessive twisting or stretching. Patients should avoid activities that may put undue stress on the implanted components of the Altius System. Activities that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching can cause component fracture or dislodgement. Component fracture or dislodgement may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component. Patients should avoid excessive bending of the torso.

Component manipulation by patient. Patients should avoid manipulating or rubbing the Altius IPG through the skin. Manipulation may cause component damage, cuff dislodgement, skin erosion, or stimulation at the implant site.

Scuba diving or hyperbaric chambers. Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA). Pressures below 10 meters (33 feet) of water (or above 2.0 ATA) could damage the Altius System. Before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their physician.

Walking or standing with prosthesis. Do not start or use Altius treatment while walking or standing with prosthesis. Any sudden response to treatment may interfere or impair ability to stand or walk.

Massage Therapy. Patients should avoid receiving massage therapy near the implanted Altius components. If patients receive massage therapy, inform the massage therapist about implanted device and show them where the IPG and cuff electrodes are located. These areas should be avoided during a massage.

Unexpected changes in stimulation. Electromagnetic interference, postural changes, and other activities may cause a perceived increase in stimulation, which some patients have described as uncomfortable stimulation (jolting or shocking sensation); therefore, patients should turn off stimulation before engaging in activities that could be unsafe for themselves or others if they received an unexpected jolt or shock (eg, driving, operating power tools). Patients should discuss these activities with their physician.

1.7. Component disposal

When explanting Altius System components (e.g., replacement, cessation of therapy, or postmortem), or when disposing of accessories, follow these guidelines:

- If possible, return the explanted component with completed Return Authorization documents to Neuros Medical for analysis and disposal.
- To allow for component analysis, do not autoclave the component or expose the component to ultrasonic cleaners.
- Dispose of any components not returned to Neuros Medical according to local environmental regulations;

Precautions:

- Follow appropriate biohazard controls for all explanted components or components coming into contact with bodily fluids. Only return such components to Neuros Medical in the appropriate packaging supplied by Neuros.
- Do not incinerate or cremate the Altius IPG because it may explode if subjected to these temperatures.

1.8. Patient selection

Best results of Altius System therapy are achieved when the patient is fully informed about the therapy risks and benefits, surgical procedure, follow-up requirements, and self-care responsibilities.

Maximum benefits from the Altius System require long-term postsurgical management.

The Altius System is not suitable for every patient with chronic intractable post-amputation pain. Suitable candidates for Altius have:

- Unilateral lower limb amputation.
- Moderate to severe chronic post-amputation pain, including residual limb and/or phantom limb pain.
- Adequate response to anesthetic injection for regional nerve block.
- Ability to operate the system.

The safety and effectiveness of the Altius System has not been established for:

- Pregnant women (including effects on a fetus, or during childbirth)
- Pediatric use (patients under the age of 22)

1.9. Long term effectiveness of Altius System

Long-term clinical data regarding the effectiveness of the Altius System is not yet available.

2. Adverse events summary

The implantation of the Altius System involves risks that are similar to other surgical implant procedures. In addition to those risks associated with surgery, the following adverse events may occur with implantation or use of the Altius System. Certain adverse events may necessitate surgical intervention.

- Undesirable response to electrical treatment, for example: pain, discomfort, undesirable sensation (incl. numbness, and tingling), and stimulation of surrounding tissue (incl. nerves and muscle)
- Heating pain or tissue injury during battery charging
- Falling or other unintentional response due to sudden change in treatment
- Infection, cellulitis, abscess, fever, and sepsis

- Immune or inflammatory response to any of the implanted materials or components, for example: rejection, skin irritation, rash or redness, allergic reaction, dermatitis, inflammation, granuloma, and itching
- Skin breakdown, for example: poor healing, wound reopening, pressure sores, and erosion at location of implanted components (IPG, Leads)
- Stiffness and decreased range of motion
- Pain, for example: pain near implanted components, phantom sensation or pain, and neuroma pain
- Malfunction of device which may result in loss of treatment, for example: dislodgement, breakage (incl. fragments), loose connections, electrical shunt, short or open circuits
- Early life failure of the IPG battery, necessitating removal or replacement.
- Nerve injury and neuropathy (numbness, pain and tingling) including compression injury
- Interference with prosthesis
- Radiation exposure if diagnostic x-rays are needed
- Adverse effects as a result of MRI or diathermy.
- Changes in blood glucose levels in response to any adverse effect.

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

For adverse events observed in Altius clinical studies, refer to the Clinical Summary.

If a serious incident related to a patient's therapy occurs, immediately report the incident to Neuros Medical and the applicable competent authority.

3. Patient counseling information

Physicians should provide patients and caregivers with information about:

- The components of the Altius System: cuff, extension, and IPG.
- Instructions for using the Altius System, including use of the patient controller to initiate a 30-minute therapy session as needed to control pain, and use of the battery charger to recharge the IPG.
- The indications, contraindications, warnings, precautions, and adverse events for the Altius System.
- Physicians should also instruct patients to:
- Always inform any health care personnel that they have an implanted Altius System before any procedure is begun.
- Contact their physician if they notice any unusual symptoms or signs.

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Appendix I: Electromagnetic Interference for Information on Sources of EMI

Please review Electromagnetic interference (EMI) under "Warnings" in section 1.4 and Table 1: Potential effects of EMI from equipment or procedures on page 7.

Before any medical procedure is begun, patients should always inform any health care personnel that they have an implanted Altius System. The potential for the following effects results from an interaction of the Altius System and equipment —even when both are working properly.

Warnings

EMI from the following medical procedures or equipment may damage the device, interfere with device operation, or cause harm to the patient. If these procedures are required, follow the guidelines below:

Diathermy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the Altius System. Medical diathermy is generally contraindicated in patients with implanted devices. The effects of such intense energies on the Altius IPG cannot be predicted.

The energy generated by diathermy can be transferred through the Altius System, possibly causing tissue injury, severe injury, or death. The Altius IPG, whether on or off, may be damaged.

Although damage to the circuitry of the IPG appears unlikely, it nevertheless could occur. If diathermy is to be used notwithstanding the risk, it may not be applied in proximity of the Altius IPG and its leads, (i.e. as far away as possible is recommended). The risk of adverse effects can be decreased by ensuring that no therapy treatment session is in progress. The Altius IPG may revert into “Down” Mode, and it will have to be reset.

All patients should be advised to inform their healthcare professionals that they should not be exposed to diathermy treatment.

Electrocautery. High-voltage, high-frequency current used to stop bleeding during surgery or as a result of trauma. If necessary, bipolar electrocautery is recommended and to ensure no therapy treatment session is in progress.

Use of surgical electrocautery devices, high-voltage, high-frequency current, can induce Altius IPG signal inhibition or can make the IPG revert to its “DOWN” mode, with no delivery of therapy. The device can be damaged if high energies are coupled into the system.

Use of electrocautery in close proximity to an implanted Altius System IPG can also couple radio frequency energy directly through the leads into the abdominal tissue, producing burns.

If electrocautery is used, it is recommended that bi-polar electrocautery is used, not uni-polar electrocautery. If the Altius IPG reverts to its “Down” mode, it will have to be reset.

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RF nerve lesioning. Radio frequency (RF) electromagnetic energy to interrupt nerve conduction as a treatment for chronic neck and spine pain.

If the procedure is required, it should be done as far from the Altius IPG as possible, and to ensure no therapy treatment session is in progress.

Use of RF Nerve lesioning may damage or cause unpredictable operation of the IPG. If the Altius IPG reverts to its "Down" mode, it will have to be reset.

Defibrillation Cardioversion. Defibrillation Cardioversion is where high voltage paddles to stabilize the heart rhythm during life threatening ventricular fibrillation or pulseless ventricular tachycardia in an emergency. Any implanted device can be damaged by external cardioversion or defibrillation. The defibrillation current can make the Altius IPG revert to its "DOWN" mode. The system can be damaged by exposure of high energies. No particular paddle placement can avoid such damage. To decrease the risk, it is recommended to position the paddles as far away from the Altius IPG as possible. In addition, paddle positions that would bring the Altius IPG into the direct path of the defibrillation current should be avoided. In the unlikely event of abnormal function, reprogramming of the IPG may be required. If the device is found to have reverted to its "DOWN" mode, it needs to be reset.

Radiation therapy. Can lead to a wide spectrum of effects, reaching from transient interference to permanent damage. It is therefore advisable to locally shield the Altius IPG against radiation if radiation therapy is to be used. If tissue in the vicinity of the implant has to be irradiated, it may be advisable to relocate the IPG.

WARNING: Therapeutic equipment generating ionizing radiation, such as linear accelerators and cobalt machines employed for treating malignant diseases, can damage the circuits used in most active implantable devices. Because the effect is cumulative, both dose rate and total dose determine if damage will occur and its possible extent. Please be aware of the fact that certain types of damage may not be immediately obvious. In addition, the electromagnetic fields generated by some types of radiation equipment for beam "steering" purposes can affect the function of the Altius IPG.

Lithotripsy. Lithotripsy is a therapy where high energy shock waves are used to treat stones in the kidney, bladder, ureter or gall bladder ultrasonic scanning. These very high frequency sound waves used to produce images of internal organs or tissue for diagnostic purposes.

WARNING: Direct exposure of the Altius System IPG to shock waves can damage the device. A device implanted outside the shock wave path presents no clearcut contraindication to lithotripsy. Before a lithotripsy is used, the patient should ensure that no therapy treatment session is in progress. If the device is found to have reverted to its "DOWN" mode, it will need to be reset.

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High-output ultrasound. High frequency sound waves which may be applied as physical therapy to treat certain bone and muscle injuries, for muscle therapy, or to improve blood. If therapeutic Ultrasound is to be used, it should not be applied in the region of the Altius IPG. If the patient cannot use therapy, then the IPG should be checked, as it may need to be reset.

WARNING: Direct exposure of the Altius System IPG to therapeutic ultrasound can damage the device. In addition, unexpected focusing of the ultrasound beam may harm the patient.

Transcutaneous Electrical Nerve Stimulation (TENS). TENS is generally contraindicated in patients with implanted electrical devices. The high-voltage impulse delivered into the body by the TENS unit can impair the operation of the Altius System IPG. If a TENS unit is used nonetheless, the TENS electrodes have to be attached as far as possible from the Altius System IPG and the Cuff Electrodes. In addition, aiming for a limited current path, the TENS electrodes should be placed as close to each other as possible. Ensuring that a therapy treatment session is not in progress reduces the risk of adverse effects.

Precautions

EMI from the following equipment is unlikely to affect the Altius System if the guidelines below are followed. Consult other equipment manufacturer's product labeling for additional guidance.

Environmental conditions

Household items. Most household appliances and equipment that are working properly and grounded properly will not interfere with the Altius System. Many household items contain magnets or generate magnetic fields that are strong enough to activate the magnet switch inside the IPG, which can be programmed to start or stop therapy.

Home and commercial microwave ovens do not affect the operation of the Altius IPG, provided they are in good condition and used as intended. Even microwave energy from a severely defective microwave oven directly radiating onto the IPG should not damage the device, Patients with an implanted Altius IPG should be advised that some electric razors, electric power tools, and electric ignition systems, including those of gasoline powered engines, could cause interference. Generally, patients implanted with an Altius IPG may use gasoline powered engines, provided that protective hoods, shrouds, and other shielding devices have not been removed.

If interference is suspected, instruct the patient to move away or turn off the household item.

Store Anti-Theft Systems/Airport Security Screening Systems. Certain types of anti-theft systems, such as those installed at entrances/exits of stores, libraries and other facilities, as well as airport security systems can interfere with the Altius System IPG. Such interference would most often inhibit therapy signal delivery, if there is a therapy session in progress. Patients should be advised to proceed through such systems at a normal pace, i.e. not to slow down while passing through. Prior to passing through airport security systems, patients should notify the attendant security personnel that they carry an implant and should present their implant ID card.

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Industrial Machinery. High voltage power lines, electric and arc welders, electric smelters, and power generating equipment can interfere with the operation of the Altius System IPG. For that reason, one needs to take into account the field strengths and modulation characteristics of all electromagnetic fields patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, and how they can minimize them by not running therapy treatment sessions when they are around these devices.

Transmitting Devices. Communication equipment such as radio and TV transmitters (including amateur ["ham radio"] transmitters, microwave, and CB radio transmitters with power amplifiers) as well as radar transmitters can interfere with the operation of the Altius System IPG. For that reason, one needs to take into account the field strengths and modulation characteristics of all electromagnetic fields patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, and how they can minimize them by not running therapy treatment sessions when they are around these devices.

Cellular and Mobile Phones. Cell phones and other mobile phones can affect the operation of the Altius IPG. These effects can be caused by the radio frequencies emitted by the phones or by the phones' speaker magnets. Potential effects include inhibition of or inappropriate Altius signal delivery if the phone is in very close proximity (within 30 cm / 12 in) of an Altius IPG and the corresponding leads. Because of the great variety of mobile phones as well as the significant physiologic differences between patients, it is impossible to make generally applicable recommendations. As a general guideline, patients implanted with an Altius IPG who would like to use a mobile phone are advised to hold the phone to the ear that is contralateral to the implant site. Patients should not carry the phone in a breast pocket or on a belt closer than 25 cm (10 in) from the implanted IPG because some phones emit signals even when they are turned on but not in use.

Compared to smaller cell phones, portable (handbag) and mobile (permanent car or boat installation) phones will generally transmit at higher power levels. For phones with higher transmission power levels, it is recommended to maintain a minimum separation of 50 cm (20 in) between the antenna and the implanted IPG.

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Appendix II: Federal Communications Commission (FCC)

The Altius Patient Controller and the Altius IPG:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

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

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

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

The Altius Programmer Wand:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class A digital device, pursuant to part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference when the equipment is operated in a commercial environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference in which case the user will be required to correct the interference at his own expense.

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

ALTIUS SYSTEM PRESCRIBER INSTRUCTIONS FOR USE

The Altius Battery Charger:

This Device Complies with Part 18 of the FCC rules.

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.

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

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.

Altius® Direct Electrical Nerve Stimulation System - Implantable Pulse Generator and Cuff Electrode Lead Implant Manual and Instructions for Use

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

LB-0198 Rev B

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Neuros Medical (USA), Inc
26800 Aliso Viejo Parkway, Suite 250
Aliso Viejo CA 92656, USA
Support Phone Number: 833-240-4462

The information provided in this document may change without prior notice.

Please read the complete documentation provided before you use the device.

Although FDA has determined that the probable benefits outweigh the probable risks, there remains some uncertainty regarding the manufacturer's human factors engineering (HFE) and usability engineering (UE) analysis and validation testing. As a condition of approval, FDA is requiring the manufacturer to provide an HFE/UE analysis and validation testing and recommending that this analysis and testing is designed using the FDA's 2016 guidance document "Applying Human Factors and Usability Engineering to Medical Devices" (https://www.fda.gov/media/80481/download).

This manual can also be found at: www.neurosmedical.com

The Altius® System is protected by several U.S. Patents.

For an up-to date list of relevant patents and patent applications, visit our patents page: https://www.neurosmedical.com/patents

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Table of Contents

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Table of Figures

Refer to the Prescriber manual for indications, contraindications, warnings, precautions, adverse events summary, individualization of treatment, patient selection, use in specific populations, and component disposal.

This product manual covers implant instructions for Altius. Refer to the Programming manual and Patient User manual for additional instructions for use, including information on using the Programming Wand, Patient Controller, and Battery Charger.

For information that supports the clinical use of the Altius System, refer to the clinical summaries manual.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

1. Explanation of Symbols

Symbol	Symbol Meaning
	**Model Number**
	**Quantity**
	**Serial Number**
	**Unique Device Identifier**
	**Consult Instructions for Use**
	**Refer to Instructions for Use**
	**Caution**
	**Magnetic Resonance (MR) unsafe**
	**Do Not Use if Package is Damaged**
	**Temperature Limitations for Transport & Use**
	**Prescription only**
	**Medical Device**
	**Non- Ionizing Electromagnetic Radiation**
	**Humidity**
	**Atmospheric Pressure**
	**Keep Dry**
	**Keep Out of Sun**
	**Type BF Applied Part**

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Symbol	Symbol Meaning
IP22	**Liquid Ingress Protection**
	**Manufacturing Date**
	**Manufacturer**
	**Battery Charger Data Port – Not for Patient Use**
	**Battery Charger Power Port**
	**Battery Charger Symbol**
	**IPG Symbol**
	**Battery Charger Signal Strength Indicator**

2. Altius System Overview

2.1. Description of Altius Direct Electrical Nerve Stimulation System

The Altius System consists of an Implantable Pulse Generator (IPG), Cuff Electrode(s) with two bands of circumferential contacts, surgical tools and accessories, Programmer Application Software, and Programmer Wand; The patient will be supplied with a Patient Controller, and Battery Charger with charging paddle.

The Altius System IPG, Cuff Electrodes and accessories are intended to be used as on-demand therapy to aid in the management of chronic intractable phantom and residual lower limb post-amputation pain in adult amputees, as detailed in the Altius Prescriber manual (LB-0195). Refer to the Altius Prescriber manual for indications, contraindications, warnings and precautions, as well as other important device and patient care information.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

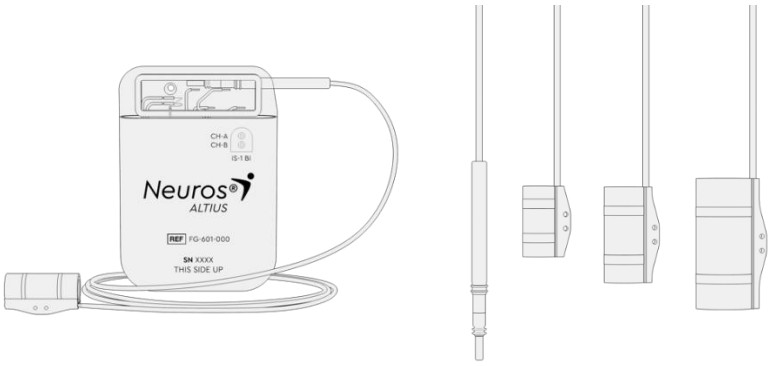

Figure 1: IPG and Cuff Electrode Connector and Three Cuff Sizes

The *implantable components* of the Altius System are:

- Implantable Pulse Generator (IPG)
- Implantable Cuff Electrodes

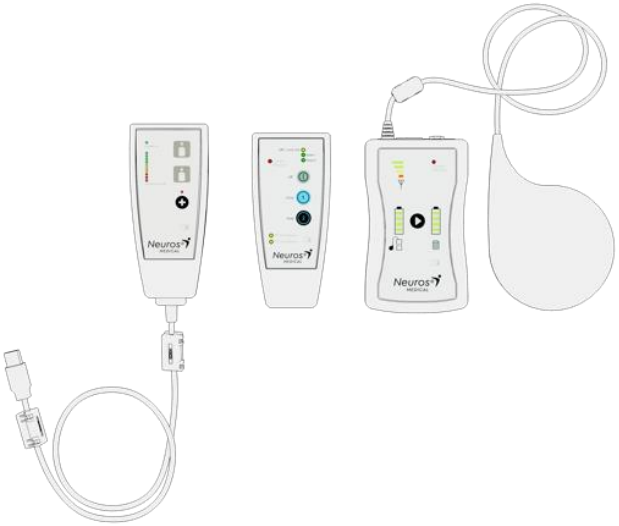

Figure 2: Non-Implantable Altius Components

The *non-implantable components* of the Altius System are:

- Battery Charger
- Patient Controller
- Programmer Wand
- PAPC Programmer Application Personal Computer (not shown in figure 2. Refer to Programmer Manual))

2.2. Altius System IPG Physical Characteristics

The Altius IPG is designed to deliver electrical stimulation to nerves. The electrical signals travel from the IPG, through the lead wire, to Cuff Electrodes placed circumferentially around the nerve(s). The physical characteristics of the Altius IPG are outlined in the table below:

Description	Value[a]
Height	68.5 mm
Width	47.0 mm
Thickness	11.0 mm
Volume	34 cm^3
Mass	60 g
Number of connector ports	2
Lead connectors	3.2 mm; IS-1 Bi-polar
Battery life	10 years[b]
Power source	Lithium ion rechargeable battery[c]
Radiopaque identification (ID) code	NRS AXX[d]
Materials in contact with human tissue[e]	Titanium, Epoxy resin, Silicone rubber
Exposed metallic surface[e]	59.28 cm^2
Exposed Epoxy surface[e]	19.44 cm^2

a. All measurements are approximate.

b. For battery life see section 2.5

c. Model Contego 325mAh Lithium-ion battery (li-Ion) manufactured by Resonetics (Formerly Eagle-Picher). The battery provides a usable capacity of 325 mAh, and a Recharge rate of C/2.

d. The Altius IPG contains a unique radio-opaque identifier within the hermetically sealed case allowing X-rays to identify information about the implant. The radio-opaque identifier is 7x6 mm (roughly 0.25 inches square) and contains the acronym "NRS" for Neuros plus alphanumeric characters identifying the version and year during which the IPG was manufactured (e.g. "A12" indicates Alpha 2012).

e. Tests have revealed that these materials are biocompatible. The Altius System IPG does not cause any temperature elevation capable of damaging the surrounding tissue.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

2.3. Altius System Nerve Cuff Electrode Physical Characteristics

The physical characteristics of the Altius Cuff Electrode are outlined in the table below:

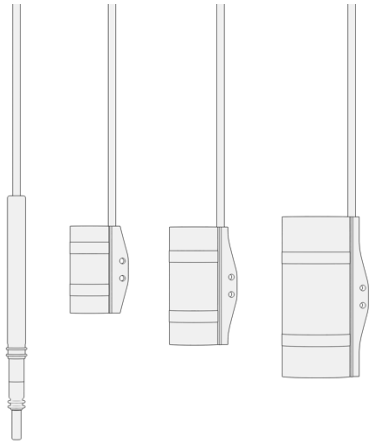

Figure 3: Connector and The three Cuff Sizes

Description	Value
Cuff Sizes (minimal diameter)	4 mm, 6 mm, 9 mm
Inner Diameter Ranges	4-6 mm, 6-9 mm, 9-13 mm
Cuff Lengths – nominal	15 mm, 20 mm, 28 mm
Number of Contact-Bands[a]	2
Contact-Band Spacing (inner edge to inner edge)	5 mm, 7 mm, 11 mm
Cable Length[a] (not incl. distal Cuff)	100 cm
IS-1 Connecter diameter – nominal	3.2 mm
Materials in contact with human tissue[a] – Platinum, MP-35N, Silicone	
[a] Tests have revealed that these materials are biocompatible.	

2.4. Altius System IPG Rechargeable Battery Behavior

The battery voltage of the Altius IPG, when its battery is fully charged, is approximately 4.1 V. When the battery voltage falls to 3.3V, the device enters RTC only, an operating mode where all circuits are disconnected except for the on board clock, battery voltage monitoring, and battery recharge signal monitoring.

If the battery drops below 3.0V, the device enters a low-power mode where the device is only listening for the battery recharge signal.

The device will return to normal behavior once the battery voltage rises above 3.3 V

It is therefore recommended to charge the IPG at least once a week. Recharging is also recommended if the device is interrogated, and the battery level is at or below 3.5V.

Additionally, patients who use the Altius IPG more frequently will require more frequent charging. Neuros Medical recommends a recharge schedule that fits the patient's personal lifestyle, while maintaining sufficient charge to deliver a complete treatment session.

Developing a patient's IPG recharge schedule involves finding the right balance between how frequently the patient wants to recharge and how long the patient wants to spend during each recharge session. Recharge time can range from between 30 minutes to approximately 6 hours. Patients should be instructed to charge until the Charger emits an end-of- charge, one-beep signal.

2.5. Altius System IPG Battery Life

The anticipated life of the IPG battery varies, depending on the IPG settings and utilization patterns over time. At typical settings, and usage and with weekly charging, the battery is predicted to last 10 years. A patient's specific utilization and settings may result in shorter or longer battery life. The Altius System utilizes voltage and frequency with a 30-min time duration to provide therapy. Based on Altius IPG's battery capacity and power requirements, a patient with a single Cuff Electrode connected to the Altius IPG, with typical values from the Table below, and running two therapy sessions a day, will use approximately 19.5 mAh over 24 hours. Over a 7-day period the IPG would consume 136.7 mAh of battery capacity, or about 40% of battery capacity, when new. The following Table provides the values for a typical use example.

Parameter	Value
Voltage	7.5 (peak voltage)
Frequency	10 kHz
Therapy Duration	30 min
Cuff Electrode Impedance	600 Ω
Therapy Current Consumption	19 mA
24-Hour IPG Battery Capacity Consumption	19.5 mAh

All Altius IPGs eventually require surgical replacement as a result of battery depletion. When the battery is depleted, communication with the IPG or continued treatment will not be possible. IPG replacement does not, in of itself, require cuff replacement unless a cuff break is suspected.

2.6. Altius System programming settings

The Altius IPG has 2 channels, Channel A and Channel B. Each Cuff Electrode, that is implanted on separate nerves, is assigned to either Channel A or Channel B respective to the IPG connector port into which it was inserted, CH-A or CH-B (see table 2). Therapy is delivered to each nerve through these channels independently.

The Altius IPG can be programmed with up to 2 doses, called Dose 1 and Dose 2, allowing patients to select and use the dose they prefer. Each dose can be programmed to deliver a programmed therapy on Channel A only, or just Channel B only, or simultaneously on Channel A and Channel B. Some parameters are in common across all Doses (1 & 2) and Channels (A & B). The range of values for these parameters is shown below:

Altius IPG Parameter Ranges		
General Parameters	**Specifications**	**Increment**
Waveform	Sinusoidal	-
Frequency (High)	5khz, 10khz	-
Channel Sequence	A First, B First	-
Lockout	0.5hr	-
Channel Delay	0 min	-
Dose/Channel Parameters	**Specifications**	**Increment**
Enabled	Yes/No	-
Initial Amplitude	0-8Vp	0.1V
Ramp Duration	0-15 min	1 min
Final Amplitude	0-16Vp	0.1V
Plateau Duration	0-30 min	1 min

At the Patient's initial activation and programming visit, to find the patient's response to Direct Electrical Nerve Stimulation their parameter settings will be determined using a 15-minute Ramp Duration which will involve the voltage will start at 0V and over the 15 minutes be increased to 15V. Using the patient's responses the parameters will then be set to achieve a sensation that is strong, but tolerable transient sensation for the patient.

Subsequent adjustment visits will be made based on the patient's ability to handle the therapy with either an increase or decrease of that therapy.

2.7. Implanted components and MRI scans

WARNING: Safety of MRI/NMRI with an implanted Altius System has not been evaluated. Patients implanted with the Altius System, or any of its components, should not be subject to MRI/NMRI. MRI exposure may result in dislodgement of the Altius IPG or Cuff Electrode(s), heating of the Altius IPG, injury to the nerve, and increased voltage through the Cuff Electrodes or Altius IPG. If MRI/NMRI is needed for any reason, the Altius System must be explanted prior to the diagnostic MRI/NMRI. For patients implanted with the Altius IPG, receiving an MRI/NMRI diagnostic scan, without first explanting the IPG may result in severe patient injury, death or device malfunction.

2.8. When explanting components

CAUTION: If permanently explanting an IPG, be sure to also explant all cuffs, leads, extensions, and accessories. Abandoned components may prevent the patient

from being allowed MRI scans in the future due to concerns of cuff electrode heating that can result in tissue damage.

3. Experience and Training

Implanting surgeons should be familiar with lower limb surgical procedures and should review the procedures described in the implant manual before surgery.

4. Handling

4.1. General

All system components and accessories should be handled with care. External devices should not be dropped, submerged in water, or operated in the rain. Avoid all sources of water that can come into contact with the external devices. Although reliability testing has been performed to ensure quality manufacturing and performance, dropping the devices on hard surfaces or in water, or other rough handling, can cause permanent damage.

4.2. Handling during Surgical Implant

Care must be taken to avoid damaging the Cuff Electrode or the Altius IPG with sharp instruments or excessive force during surgical implant. The following guidelines will help to ensure the longevity of components:

- Do not implant the Altius IPG if it has been dropped. Dropping can cause latent damage to components, loss of sterility, loss of hermeticity, or other damage. Replace the dropped Altius IPG with a new, sterile Altius IPG prior to implantation.

WARNING: If the Altius IPG case is pierced or ruptured, severe burns could result from exposure to battery chemicals.

- Do not sharply bend or kink any segment of the Cuff Electrode.
- Avoid applying excessive tensile forces in any direction and to any segment of the Cuff Electrode. During insertion of Cuff Electrode connectors into the Altius IPG header; a damaged connector may result in failure to deliver therapy
- Avoid pulling an implanted Cuff Electrode lead taut; strain relief loops may help to minimize tension on the Cuff Electrode.
- If anchoring of the strain relief loops is necessary, do not tie the anchoring sutures overly tightly as they may cut through the silicone tubing.
- Avoid handling the Cuff Electrode with sharp instruments; use only rubber-tipped forceps.
- Take care when using sharp instruments, such as hemostats or scalpels to prevent damage to the Cuff Electrode.

4.3. Storage and Handling

The Altius IPG can be stored between -30° C and 60° C (-22° F and 140° F). Neuros recommends storing the Altius IPG below 24° C (75° F). Store the Cuff Electrode between -29° C and 60° C (-20° F and 140° F. Components of the Altius System should always be kept

in temperature-regulated areas within the acceptable temperature range. Altius IPG damage can occur at temperatures outside of this range.

The Altius IPG is intended to be used between 17° C and 40° C (63° F and 104° F).

4.4. Packaging Information

Read the label on the product package before opening to ensure you have the right product. The Altius System IPG and Cuff Electrode are single use, single patient products and are supplied in a shelf box containing a literature pack and the sterile package. The sterile packs have been sterilized with ethylene oxide gas. Both the IPG and Cuff Electrode consist of an outer TYVEK/PET blister pack containing an inner TYVEK/PET blister. For products that are provided STERILE, introduce the contents into a sterile field: (1) Peel the Tyvek lid from the outer tray, (2) use a sterile handling technique to put the inner tray into sterile field, and (3) peel the Tyvek lid from inner tray to expose the contents. Before opening the sterile package, check for any signs of damage suggesting that the sterility of the package or its contents might have been compromised. Damaged packages need to be returned to Neuros Medical.

IPG Kit Contents:

Shelf box contains:

- Altius System Patient Implant Card
- Peel-off labels for use with implantation documents
- Sterile inner blister pack contains:
  - One (1) Altius System IPG
  - One (1) Allen Torque Wrench [Size - 0.035in (0.9mm), Torque - 11oz-in (77.68 mNm)]
  - One (1) Port Plug

Cuff Electrode Kit Contents:

- Shelf box contains:
- Peel-off labels for use with implantation documents
- Sterile inner blister pack contains:
  - One (1) Cuff Electrode

4.5. Re-sterilization and Reuse

The Altius IPG, Cuff Electrodes, and kit contents were sterilized with ethylene oxide prior to shipment. Check the expiration date on the package before opening the sterile package and using the contents. Do not use the contents after the expiration date, if the sterile barrier is breached, or if contamination is suspected because of a defective sterile package seal.

- Do not use any component that shows signs of damage.
- Do not use if “Use Before” date has expired.
- Do not attempt to re-sterilize the contents of the sterile package that has been damaged or in any way compromised. Return any unopened devices to Neuros Medical.
- The Altius IPG, Cuff Electrode, port plug, are single-use only devices. Do not re-implant for any reason.

- An Altius System IPG that has been explanted for any reason may not be reimplanted in another patient.

5. Device Implantation

5.1. General Considerations

This section describes the recommended procedures for implanting the Altius System for the treatment of Post-amputation Pain. Procedures discussed include Cuff placement, IPG placement, and lead wire tunneling.

Cuffs are designed for permanent implant. In single Cuff procedures, the Cuff is wrapped around the sciatic nerve 1 to 3 cm proximal to the nerve end or neuroma, if present. Single Cuff procedures are typically performed with patients who have an above the knee amputation (AKA). In two Cuff procedures, one Cuff is wrapped around the tibial nerve, and one Cuff is wrapped around the common peroneal nerve, 1 to 3 cm distal to the branch of the sciatic nerve. Two Cuff procedures are typically performed with patients who have a below the knee amputation (AKA). See section 5.2.1, Cuff Electrode Placement for additional details.

The lead wire (one Cuff procedure) or wires (two Cuff procedure) are tunneled subcutaneously from the Cuff placement site to the IPG pocket, an access incision may be used to transition and tunnel to the IPG pocket.

The IPG is placed in a subcutaneous pocket in a location in the abdomen as deemed appropriate by the implanting physician, considering the patient's ability to reach the IPG location for initiation of Direct Electrical Nerve Stimulation with the Patient Controller. It is recommended that an appropriate location be used to minimize tensile forces on the lead wire during subject movement. The patient should also be consulted to ensure that the IPG is placed such that it does not cross their belt-line.

WARNING: The IPG uses a transcutaneous wireless charging system which may result in heating. When implanting the IPG be aware of and avoid any thermally sensitive tissues.

WARNING: Use of surgical electrocautery devices, high-voltage, high-frequency current, can induce Altius IPG signal inhibition or can make the IPG revert to its "DOWN" mode, with no delivery of therapy. The device can be damaged if high energies are coupled into the system.

Use of electrocautery in close proximity to an implanted Altius System IPG can also couple radio frequency energy directly through the leads into the abdominal tissue, producing burns.

If electrocautery is used, it is recommended that bi-polar electrocautery is used, not mono-polar electrocautery. If the Altius IPG reverts to its "Down" mode, it will have to be reset.

5.1.1. Patient Pre-operative preparation

The patient should undergo a nasal swab to test for *Staphylococcus* and application of mupirocin to nares in patients who test positive.

The day before and the day of the procedure the patient should bathe with antimicrobial soap (such as Phisohex or Hibiclens).

Follow institutional protocols for pre-operative IV antibiotics.

5.1.2. Patient Preparation

- The patient is preferably placed in the Lateral Decubitus Position with the amputated limb up.
- Using standard sterile techniques, carry out the appropriate skin prepping, draping, and injection of local anesthetic to perform the implant procedure for Cuff or Cuffs.
    - Drape the patient's contralateral limb (that is in the down position) before draping the surgical site.
    - This will allow the sterile field to be maintained later in the surgery when the amputated limb is flexed at the hip to ensure there is enough slack in the lead.
- The patient should be anesthetized as per the physician's discretion.

PRECAUTIONS FOR INFECTION PREVENTION

Note: In addition to standard operating room (OR) sterile-field procedures and strictly excluding candidates with a history of surgical infections, the following steps are strongly recommended:

1. Double gloving by surgeons and Operating Room (OR) personnel.
2. Use of bio-occlusive dressings for incisions.
3. Additional recommendations throughout this section.

5.2. Cuff Electrode Implantation

WARNING: As a preventative measure, the nerve should be visualized using ultrasound and target incision location where the diameter is less than 13 mm. Ensure proper handling during dissection, measurement, and cuff placement and anchoring to prevent nerve damage.

5.2.1. Cuff Electrode Placement

- Expose and mobilize the target nerve(s) using the standard technique for a nerve sparing gentle dissection. As a general rule, the following Table is representative of standard cuff placement.

	1 Cuff Electrode	**2 Cuff Electrodes**
Nerve(s)	Sciatic	Tibial and common peroneal

NOTE: Implanting physicians may elect to place two cuffs on a bifurcated sciatic, and in some cases, a single cuff on a BKA subject (e.g., very distal tibial common peroneal bifurcation). Final decisions regarding Cuff Placement are made at the time of the surgical procedure.

- Measure the diameter of the nerve using Maquet graft sizers, vessel loops or comparable tool and select the appropriately sized Cuff.
- Soak cuff electrode(s) in antibiotic solution.
- Orient Cuff Electrode such that the lead wire from the Cuff is routed superior from Cuff.
- Protrude angled forceps out from under nerve. Gently clasp Cuff edge that has a suture anchor and pull Cuff under nerve.
- With forceps, being careful not to clasp the metal contacts, carefully wrap the Cuff edge that does not have a suture anchor around the nerve.
- Overlap the Cuff edge that has a suture anchor over top the Cuff edge without a suture anchor. Ensure there is circumferential coverage of the nerve, and that the platinum contacts are touching the nerve. After circumferentially wrapping the Cuff, both suture anchors should be accessible.

WARNING: If the cuff electrode overlaps itself, ensure that both electrode tracks are in contact with the nerve, and not in contact with each other; and that the overlapping section of the cuff is just silicone.

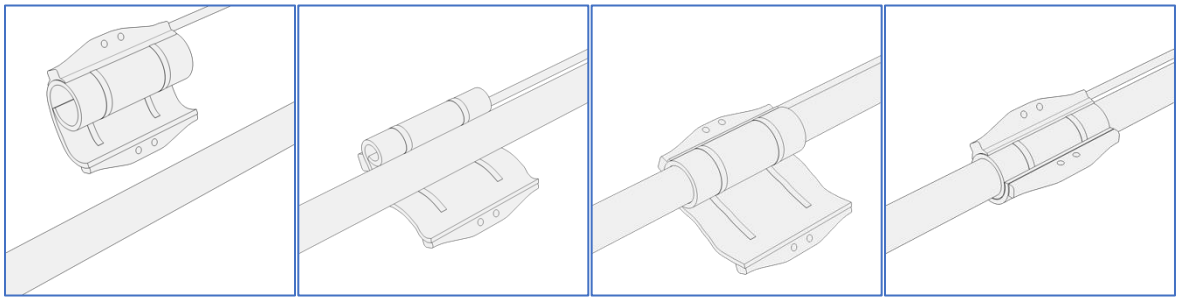

Figure 4: Wrapping Cuff Around Nerve

5.2.2. Anchoring the Cuff Electrode

- Secure the Cuff Electrode by tying a suture through the suture anchors with non-absorbable suture. Tie sutures such that the loop between the anchors remains loose. The suture is only intended to prevent unexpected unwrapping and should not be tight.

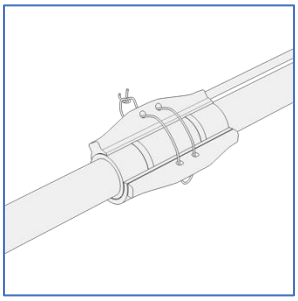

Figure 5: Secured Cuff Around Nerve

WARNING: Do not overly tighten the suture. The Cuff is self-sizing and sutures need to allow for postoperative inflammation and swelling.

WARNING: Do not suture directly through the Cuff because it may damage the Cuff Electrode.

- Flex/Extend leg to full range of motion to form slack along the cable length as necessary.
- Within the Cuff Electrode incision site, create a strain-relief loop 2-5 cm in diameter with the cable from Cuff Electrode.
- If necessary, anchor the strain-relief loop by loosely suturing through fascia and around the cable.

5.3. IPG Implantation and Cuff Electrode Connection

- Select and mark the intended Altius IPG site and create an incision at the top of the Altius IPG site. The primary location for the subcutaneous pocket is the anterolateral abdominal wall. Secondary location at surgeon discretion.
- Create a subcutaneous pocket no larger than the Altius IPG outline at a depth of no more than 2.5 cm (1 inch) from the surface.

WARNING: Shallow implant depth may lead to increase in risk of wound dehiscence leading to infection.

NOTE: It is important to keep the pocket small to reduce the chances of the IPG flipping or moving and to discourage patient manipulation. The recommended maximum depth of implant for proper device interrogation and charging is not more than 2.5cm.

NOTE: The Altius IPG device interrogation and charging could become ineffective at depths greater than 2.5cm (1 inch).

- Identify anterior superior iliac crest margin and place IPG medially to avoid the iliac crest.
- Create a small pocket beneath the left incisional border to accommodate the exiting lead from the IPG header.

5.3.1. Tunneling Cuff Electrode Lead Cable to IPG Pocket

- Mark the desired tunneling route from the Cuff Electrode incision, along the midaxillary line to the lateral abdominal wall, and then transverse to the IPG pocket.

NOTE: Avoid tunneling routes through areas that are subject to flexion to minimize the stress on the lead.

- Make a tunneling access incision in the lateral abdominal wall, where tunneling route transitions from longitudinal to transverse.
- Bend the tunneling tool to conform to the patient's body.
- Create a subcutaneous tunnel that begins inside the Cuff Electrode incision site and extends to the tunneling access incision site.

NOTE: Deep tunneling should be avoided to prevent potential injury to other tissue in the body.

Pass the Cuff Electrode connector through the sheath (or tunneling sheath), with attention to avoid reducing the diameter of the strain relief loop at the Cuff Electrode incision site. Withdraw the sheath (or tunneling sheath).

- Flex/Extend leg to full range of motion to form slack along the cable length as necessary.
- Create a subcutaneous tunnel that begins inside the tunneling access incision site and extends to the IPG pocket.
- Within tunnel access incision site, make a strain-relief loop 2-5 cm in diameter with the lead from Cuff Electrode.
- Pass the Cuff Electrode connector (proximal end) through the sheath (or tunneling sheath), with attention to avoid reducing the diameter of the strain relief loops. Withdraw the sheath (or tunneling sheath).

5.3.2. Connecting and Implanting the IPG

- Do not pre-soak the IPG in any fluid. Ensure the IPG cavity (channel port) is dry.
- Ensure the Cuff Electrode Connector is dry.
- Fully insert the Cuff Electrode connector by hand into the Altius IPG port, using the table below as reference for one vs. two Cuff Electrodes. When the connector is properly inserted, it will extend to the end of the port which can be visually confirmed through the clear epoxy header.

CH A	Sciatic	Tibial
CH B	Port Plug	Common Peroneal

- Pass the torque wrench through the septum seal into the setscrew and turn clockwise until the torque wrench "clicks," indicating the screw has been fully tightened. The wrench is torque-limited and cannot be over tightened.
- For single Cuff Electrode procedures, place a silicone Altius Port Plug into the Altius IPG port unoccupied channel (typically channel B). Check that the Port Plug is secure, but do not over tighten the set screws as they may perforate the silicone.

- Place the programmer wand in a sterile ultrasound sleeve so that the system integrity may be confirmed.
- Test impedances using the Programmer Wand and the Altius Programmer Application. Verify impedances are within expected ranges.

WARNING: A wet (blood, saline, antibiotic solution…) IPG cavity or Cuff Electrode Connector could result in erroneous impedance measurement checks. Remove any fluid from these areas and ensure a dry connection.

WARNING: Observe necessary precautions when inserting the Cuff Electrode connector in the IPG. Do not use surgical tools to insert Cuff Electrode Connector. This should be done by hand.

NOTE: If the port plug is used in CH-B, it is not necessary to tighten the setscrew as described.

- Coil any excess cable from Cuff Electrode behind the Altius IPG.
- Place the Altius IPG in the subcutaneous pocket with "THIS SIDE UP" facing towards the skin.
- Secure the Altius IPG in the pocket by suturing through the hole in the IPG header and the underlying fascia.

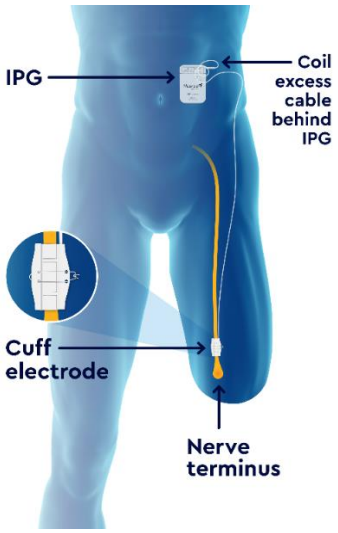

Figure 6: Implanted Altius System

5.3.3. Completing the Implant Procedure

- Lavage all surgical wound beds thoroughly with antibiotic solution.
- An antibiotic powder may be applied topically to incision sites prior to surgical wound closure.
- Close and dress all surgical wounds. Close the incisions in a transverse manner using 2 layers. The deep layer may be closed with a running 3-0 non-absorbable suture followed by an imbricating layer of absorbable 3-0 suture. Apply bio-occlusive dressing after closure.

Note: You may use either staples or suture for wound closure. If you elect to use staples, wait to activate the Altius IPG until after the staples have been removed.

5.3.4. Post-op patient care & Antibiotics

- Prescribe anti-biotics for the patient for no longer than 24-48 hours post-operatively
- If staples were used to close the incisions, ensure that the staples are removed prior to the patient's activation visit.
- Physician should discuss proper post-operative wound care with patient prior to discharge.

6. Device Explantation

In the event that the system needs to be explanted for any reason, the procedure described below is recommended to remove all implanted components. The procedure can be modified as necessary, for example to remove just the IPG in the event of IPG replacement at end of battery life.

6.1. Explanting or Replacing the Altius IPG

Turn off the Altius IPG to ensure a treatment session is not active.

Create an incision through the existing scar over the Altius IPG. The incision should extend down to the level of the Altius IPG.

CAUTION: Use bipolar electrocautery, monopolar electrocautery may damage the Altius IPG.

Withdraw the Altius IPG from the pocket.

Using a sterile Allen wrench (torque wrench), unscrew the connector setscrews to release and remove the Cuff Electrode connector(s) from the Altius IPG. While holding the IPG in one hand, grasp each Cuff Electrode silicone lead connector between thumb and forefinger. Pull the lead IS-1 connectors from the terminal by cautious application of constant traction. Grasping the plugs with a sterile pad can help improve traction. Never apply excessive traction to the actual Cuff Electrode lead body, which could damage the leads and cause lead failure.

NOTE:

- When tightening or loosening a set screw, always insert the tip of the torque wrench fully into and in line with the set screw. Do not insert the torque wrench into the set screw at an angle.
- Prior to inserting the IS-1 lead connectors, verify visually that none of the set screws protrudes into any of the IPG header cavities. Back off any set screw found protruding beyond the wall into the header cavity by turning it back in a counterclockwise direction with the Allen wrench. Turn the set screw just enough so that its tip is no longer inside the header cavity. Do not back the set screw completely out of the terminal block.
- Observe that the tips of the lead contacts are inserted beyond the respective lead tip terminals. Tighten the set screws using the sterile torque wrench included in the Altius IPG package. Turn the Allen wrench clockwise until you can clearly hear and feel the clicking that limits excessive torque on the set screw. Carefully apply traction to the strain relief of each lead to make sure that the leads are securely anchored in the terminal.

  For Altius IPG replacement, connect the new Altius IPG. Reference above section 5.3.2: Connecting and Implanting IPG.

  For the Altius System removal, continue to section 6.2: Explanting or Replacing the Cuff Electrode.

6.2. Explanting or Replacing the Cuff Electrode

Note: If the entire Altius System (Altius IPG and Cuff Electrodes) is to be removed, then the Altius IPG should be removed first (as described above) followed by the Cuff Electrodes.

- If the Altius IPG has just been explanted, cover the Altius IPG wound bed with sterile gauze moistened with normal saline while the Cuff Electrodes are explanted.
- Expose and mobilize the nerve and the electrode using the standard technique for a nerve-sparing dissection.
- Cut any sutures used to secure the Cuff Electrode.
- If two Cuff Electrodes were implanted, repeat steps 2 – 5 for the other nerve.
- Detach the Cuff Electrode from the nerve bundle by gently unwrapping the Cuff.
- Remove the Cuff Electrode using gentle traction at the distal free end of the Cuff.
- For Cuff Electrode Replacement: Prior to leaving the surgical suite, impedance should be checked and ensure the IPG is not enabled. The IPG will be enabled at the Day 14 postoperative visit.
- Close and dress all incisions.
- Note: As is required by regulation in most countries, all explanted components should be decontaminated, and returned in a sealed pouch to Neuros Medical for returned device analysis.

  All explanted Altius System IPGs should be returned to Neuros Medical Inc. for testing and analysis, which can provide valuable information on how to further improve device quality and reliability.

WARNING: Never incinerate an Altius System IPG. The battery in these devices can explode if placed in fire.

WARNING: The IPG must be explanted before a deceased patient is cremated.

WARNING: Implantable parts are not to be reused if they have previously been implanted in another patient.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Appendix I: Replaceable Parts & Cables

The Altius System is fully replaceable, there are no User serviceable parts.

For replacement of any part of the Altius System please contact your Neuros Medical Representative.

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

Non-Implantable replaceable Components:

Neuros Medical Part Name	Expected Service Life	Neuros Medical Part Number	Cable Length (If Applicable)
Altius Patient Controller	5 Years	FG-604-000	N/A
Altius Battery Charger	5 Years	FG-603-000	61cm (24in) (Charger to Paddle)
AC Adapter for Altius Battery Charger	5 Years	PC-200-044	170cm (66 in)
Altius Programmer Wand	5 Years	FG-606-000	305cm (10ft)
Programmer Application PC (PAPC)	5 Years	FG-608-000	N/A

Implantable replaceable Components

Neuros Medical Part Name	Neuros Medical Part Number	Cable Length (If Applicable)
Altius IPG*	FG-601-000	N/A
Cuff Electrode Small	FG-600-001	100cm (39 in)
Cuff Electrode Medium	FG-600-002	100cm (39 in)
Cuff Electrode Large	FG-600-003	100cm (39 in)

*The battery in the Altius IPG has undergone simulated bench tests to demonstrate battery longevity at nominal settings and usage is 10 years.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Appendix II: Wireless Specifications of the Altius System

Communication/Telemetry and Wireless Charging:

Patient Controller and Programming Wand to the IPG(Communication)

- Modulation: ASK (Amplitude Shift Keying)
- The Amplitude is 0 and a 1 is 305µs signal
- Transmit Frequency: 20kHz
- Power: 0.27 Watts (W)

Battery Charger to Altius IPG (Charging)

- Modulation: PWM (Pulse Width Modulation) (Only for limited communication)
- The pulses are 1.07ms for a 0 and 3.36 ms for a 1 (Only for limited communication)
- Transmit Frequency (386kHz – 490kHz)
- Transmitter Power is 0.52 W

Altius IPG to the Patient Controller and Programming Wand (Communication)

- Modulation: PPM (Pulse Position Modulation)
- The position between two pulses for a 0 is 183µs, a 1 is 275µs
- Transmit Frequency: 19kHz
- Power: 1.8 mW

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Appendix III: Electromagnetic Interference Information

The Altius System can be used in 4 main configurations and used accordingly as listed below:

1) The Battery Charger Being Charged by AC Mains
2) The Battery Charger Being Used to Charge the IPG Battery
3) The Patient Using the Controller to turn the IPG On/Off*
4) The Programmer System Being Used to Program the IPG

*Due to practical limitations of testing, configuration 3 and configuration 4 were determined to be equivalent to each other as the Patient Controller and Programmer Wand use the same circuitry for transmitting and receiving telemetry data.

The Altius System was found to be complaint following the testing listed below for the specified configurations and environments as specified below:

Test Standard	Configuration	Compliance Level	Electromagnetic Environment Guidelines
CISPR 11 Radiated Emissions	1,2,3	Group 1 Class B	The Altius System uses RF energy only for its internal function; therefore, its RF emission are low and ae not likely to cause any interference in nearby electronic equipment. The Altius IPG, Battery Charger and Patient Controller 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.
CISPR 11 Radiated Emissions	4	Group 1 Class A	The Altius Programmer System is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
CISPR 11 Conducted Emissions	1	Group 1 Class B	The Altius Battery Charger 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.
IEC 61000-3-2 Harmonics	1	Harmonics Class A	
IEC 61000-3-3 Flicker	1	4% max	
IEC 61000-4-2 ESD Immunity	1,2,3,4	±8kV Contact; ±2,4,8,15kV Air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, relative humidity should be 30% or higher. The operator may have to reset the system if the communication between the Programmer Wand and the PAPC is interrupted.
IEC 61000-4-4 EFT Immunity	1	±2kV 100kHz repetition frequency	The Battery Charger is suitable for use in all establishments. Including domestic

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Test Standard	Configuration	Compliance Level	Electromagnetic Environment Guidelines
IEC 61000-4-5 Surge Immunity	1	±0.5,1kV Line to Line; ±0.5,1,2kV Line to Ground	establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
IEC 61000-4-6 Conducted RF Immunity	1,2,4	3Vrms 0.15 – 80MHz; 6Vrms in ISM and Amateur Radio Bands; 80% 1kHz AM	Portable and mobile RF communications equipment should not be used at levels as tested per the compliance levels listed in the table below.
IEC 61000-4-3 Radiated RF Immunity	1,2,4	10V/m 80MHz – 2.7GHz 80% 1kHz AM	
IEC 61000-4-8 Power Frequency Magnetic Field Immunity	1,2,3,4	30A/m 50/60Hz	The Altius Programmer System is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes. The Altius IPG, Battery Charger and Patient Controller 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.
IEC 61000-4-11 VDI Immunity	1	0% UT for 0.5 Cycle at 0,45,90,135,180,225,270,315 degrees 0% UT for 1 Cycle 70% UT for 30 Cycles 0% UT for 300Cycles	The Battery Charger 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. **Note:** If the user of the Altius Battery Charger requires uninterrupted operation during power mains interruptions, it is recommended to power the Altius Battery Charger from an uninterruptible power supply or battery.
IEC 60601-1-2 ed4.1 Proximity Radiated RF Immunity (Table 9)	1,2,4	See Table 9 Compliance Levels on next page	The separation distance between an interfering RF transmitter and any Altius System Device should be greater than 0.3m (12in) and the maximum power from the RF transmitter should not exceed 2 W or 28V/m at a distance of 0.3m.
IEC 60601-1-2 ed4.1 Proximity Magnetic Field Immunity (Table 11)	1,2,3,4	30kHz CW 8A/m 134.2kHz 2.1kHz PM 65A/m 13.56MHz 50kHz PM 7.5A/m	The separation distance between an interfering magnetic field and the Altius System should be greater than 15cm, unless intentionally activating the magnetic reed switch of the IPG to deactivate therapy.

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Table 9 from IEC 60601-1-2 ed4.1 Compliance Levels:

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

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

Appendix IV: Federal Communications Commission (FCC)

The Altius Patient Controller and the Altius IPG:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

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

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

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

The Altius Programmer Wand:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class A digital device, pursuant to part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference when the equipment is operated in a commercial environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference in which case the user will be required to correct the interference at his own expense.

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

ALTIUS SYSTEM IPG AND CUFF ELECTRODE IMPLANT MANUAL AND INSTRUCTIONS FOR USE

The Altius Battery Charger:

This Device Complies with Part 18 of the FCC rules.

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.

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

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.

Altius® Direct Electrical Nerve Stimulation System Implantable Pulse Generator Programmer Manual

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

LB-0197 Rev B

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

Neuros Medical (USA), Inc
26800 Aliso Viejo Parkway, Suite 250
Aliso Viejo CA 92656, USA
Support Phone Number: 833-240-4462

The information provided in this document may change without prior notice.

Please read the complete documentation provided before you use the device.

Although FDA has determined that the probable benefits outweigh the probable risks, there remains some uncertainty regarding the manufacturer's human factors engineering (HFE) and usability engineering (UE) analysis and validation testing. As a condition of approval, FDA is requiring the manufacturer to provide an HFE/UE analysis and validation testing and recommending that this analysis and testing is designed using the FDA's 2016 guidance document "Applying Human Factors and Usability Engineering to Medical Devices" (https://www.fda.gov/media/80481/download).

This manual can also be found at: www.neurosmedical.com

The Altius® System is protected by several U.S. Patents.

For an up-to date list of relevant patents and patent applications, visit our patents page:
https://www.neurosmedical.com/patents

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

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Refer to the Prescriber manual for indications, contraindications, warnings, precautions, adverse events summary, individualization of treatment, patient selection, use in specific populations, and component disposal.

This product manual covers programming instructions for Altius System, including information on the Clinician Programmer and Altius Programming Software. Refer to the Implant manual and Patient User manual for additional instructions for use, including device descriptions, package contents, device specifications, product-specific warnings and precautions, information on using the Patient Controller, and Battery Charger.

For information that supports the clinical use of the Altius System, refer to the clinical summaries manual.

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

1. Explanation of Symbols

Symbol	Symbol Meaning
	**Model Number**
	**Serial Number**
	**Quantity**
	**Universal Device Identifier**
	**Consult Instructions for Use**
	**Refer to Instructions for Use**
	**Caution**
	**Do Not Use if Package is Damaged**
	**Temperature Limitations for Transport & Storage**
	**Humidity**
	**Atmospheric Pressure**
	**Prescription only**
	**Medical Device**
	**Type BF Applied Part**
	**Non- Ionizing Electromagnetic Radiation**
	**Keep Dry**
	**Keep Out of Sun**
	**Manufacturing Date**
	**Manufacturer**

2. Altius Programmer System Overview

2.1. Description of Altius Programmer System

The Altius Programmer System allows the physician or clinical user to interrogate and program the Altius IPG. The Altius programmer software runs on a laptop PC connected to the programming wand. Communication between the Programmer system and the Altius IPG is accomplished with the programmer wand placed directly over the implant site. The Programmer Wand communicates via magnetic induction telemetry with the Altius IPG implanted in the patient.

Understanding the instructions contained in this manual on how to operate the Altius Programmer System is essential to proper programing and operation of the Altius IPG. (Refer to the Altius Prescriber IFU for more information)

Figure 1: Altius Programming Laptop PC

WARNING: The Altius Programmer may be subject to interference from other electrical devices operated in the vicinity. Portable and mobile RF equipment is especially likely to impair the normal function of the programmer. If the Altius Programmer is not operating as expected, consider whether such interference is the cause. Other Equipment, even if performing per the specifications and within emission limits, may interfere with the Altius Programmer.

2.2. Programmer Functions

The programmer can perform the following functions:

- Read (Interrogate) Altius IPG parameters as currently programmed
- Modify Altius IPG parameters
- Retrieve the on-board log file from the Altius IPG
- Record the list of commands that are sent to the Altius IPG from the programmer
- Order the IPG to measure the Impedance of the Cuff Electrode(s) and the nerve cuff interface
- Set the onboard clock of the Altius IPG
- Single pulse - For use in determining sensory threshold for a patient
- Start and stop therapy

2.3. Programmer Components

The Altius Programmer System consists of:

- Altius Programmer Wand
- Altius Programmer Application PC
    - Altius Programmer Application installed on a Laptop PC (PAPC)
    - Laptop PC power supply
      Note: The manual for the laptop PC is also provided

WARNING: Use of items other than those identified above or in a manner not in accordance with these instructions may cause damage to the Altius Programmer.

2.4. Interconnecting the Programmer components for Operation

- Unplug the Programmer Application PC (PAPC) from its power supply.
- Plug the USB connector of the Programmer Wand into a USB port on the PAPC.

WARNING: Do not attempt to connect any line-powered device (such as a cable-connected printer) to the Altius Programmer. This may create an electrical safety hazard for the patient.

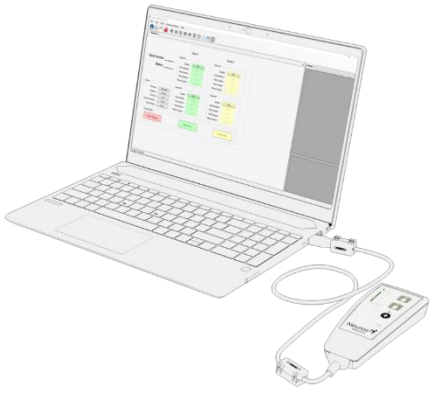


Figure 2: Altius Laptop PC and Programmer Wand

2.5. Programmer Wand

The programmer wand has three buttons:

- Interrogate
- Program
- Reset/Emergency Program – Set the parameters to default off settings

The programmer wand also has three different sets of indicator lights:

- The power indicator light, located above the text “power on”, is illuminated when the programmer wand is powered.
- The bar graph indicator lights display the strength of the telemetry signal between the Programmer Wand and the Altius IPG
- The Reset/Emergency Program indicator light, located above the Reset/Emergency program button, flashes a few times after the Reset programming has been successfully completed.

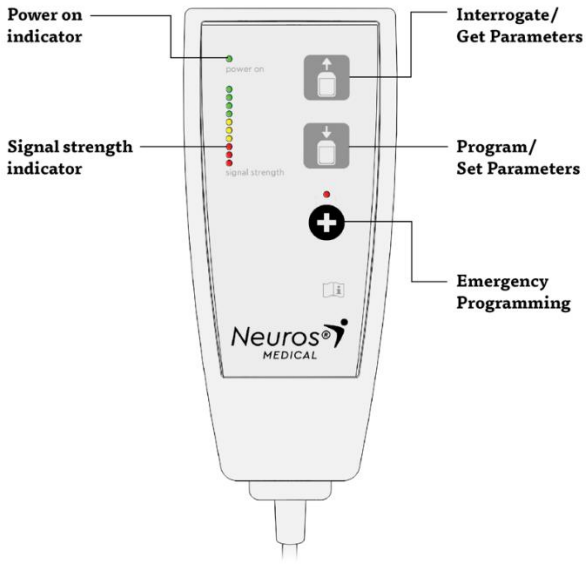


Figure 3: Programmer Wand

2.6. Charging the Battery of the Altius PAPC

WARNING: Only charge the Altius PAPC with the supplied power supply. Do not attempt to recharge the PAPC's battery with any other power supply.

To charge the battery of the Altius PAPC:

NOTE: The Power Supply main come in two separate sections 1) AC power cord and 2) AC/DC power supply and DC output connector. If this is the case, plug the two in together before starting

- Plug the DC output connector of the supplied power supply into the input power connector of the PAPC.
- Plug the other end of the power supply into AC mains wall receptacle. Be sure that the mains voltage is in the range of 100-240VAC, 50/60Hz and that the receptacle is properly grounded.

WARNING: Do not plug the Power Supply into an extension cord or other such device, only plug the power supply into a wall receptacle. Doing so may result in an electrical hazard to the device or the user.

- When charging the battery of the Altius PAPC, allow the internal battery a minimum of a 4 hour charging session before attempting to use the Altius PAPC at implant. It is recommended that the Altius PAPC battery of the Programmer System be routinely charged between uses.

2.7. Operating the Altius Programmer System

WARNING: The Altius Programmer shall not be used on board aircraft without prior consent from the aircraft's crew.

NOTE: Consult local regulations if using the Altius Programmer outside of the country where it was obtained.

CAUTION: The Altius Programmer must be operated as a battery-powered device, as there may be a risk of electrical shock to the patient from the AC mains.

NOTE: Connect it to the AC mains only when charging of the PAPC is required. The Altius PAPC should be positioned such that disconnecting it from the power supply is not impeded.

NOTE: It is recommended that you have an Altius Patient Controller on hand during programming sessions as a back-up to terminating therapy.

2.8. Using the Altius PAPC Touch Screen (If Available)

Some base laptop PC models used for the Altius PAPC may be equipped with a touchscreen. Selections on the screen may be made by touching the screen with one's finger or a stylus (may be supplied with the Altius PAPC).

CAUTION: Using sharp items or regular writing equipment (pen or pencil) may damage the touch screen.

2.9. Buttons and Symbols on the Altius PAPC

The base laptop PCs which are used for the Altius PAPC come with a Windows QWERTY keyboard layout. There will also be a separate power button.

2.10. Altius PAPC Battery Replacement

The Altius PAPC is powered by a battery that may need to be replaced if it fails to properly recharge. Contact your local Neuros Medical representative if a replacement battery is needed.

Warning: Proper disposal of the used battery is essential. Dispose of the used battery in accordance with local environmental laws and regulations.

WARNING: Never puncture or incinerate a used battery.

2.11. Routine Cleaning

WARNING: DO NOT attempt to sterilize an Altius Programmer Wand or Altius PAPC because any sterilization method could severely damage the equipment.

WARNING: DO NOT submerge any part of the Altius Programmer Wand or Altius PAPC in water. Damage to the unit may result. The Altius Programmer System is not protected against ingress of water and may have limited humidity ingress protection (IPX0).

WARNING: Always turn off and unplug the Altius PAPC and Altius Programmer Wand prior to cleaning.

Following each use, it is recommended that a soft cloth dampened with a germicidal cleaning solution be used to wipe the exterior of the Programmer Wand, and the Altius PAPC. Do not use solvents or cleaning cloths impregnated with chemical cleaning agents.

2.12. Storage, Handling and Usage

The Altius IPG and the Cuff Electrode(s) are permanent implants, they are intended to be able to be used in the home and hospital and general environment implanted in the patient. The Patient Controller and the Battery Charger are intended to be used in the home or general environment, while the programmer system, including the Programmer Wand is intended for use in the professional healthcare environment such as a hospital, clinic, or doctor's office.

The Altius Programmer Wand is designed to function normally after it has been exposed (While packaged for transport) to the following environmental extremes of -30° C and 60° C (-22° F and 140° F), relative humidity between 15% and 90%; and atmospheric pressure between 500 hPa and 1060 hPa.

The Altius PAPC is designed to function normally after it has been exposed (While packaged for transport) to the following environmental extremes of -20° C and 60° C (-4° F and 140° F), relative humidity between 20% and 75%; and atmospheric pressure between 500 hPa and 1060 hPa

Recommended conditions for normal use of the Programmer wand is 10° C and 40° C (50° F and 104° F), relative humidity between 20% and 75%; and atmospheric pressure between 700 hPa and 1060 hPa.

WARNING: When using the Programming Wand in an environment that is 40˚C (104˚F), the Programming Wand may warm up to 43.3˚C (110˚F). Ensure to inform the patient of this. If you or the patient feel any part of the system getting to hot, stop using the Programming Wand and wait for it to cool down.

Recommended conditions for normal use of the PAPC is 5° C and 35° C (41° F and 95° F), relative humidity between 20% and 75%; and atmospheric pressure between 700 hPa and 1060 hPa.

WARNING: The Altius Battery Charger and Patient Controller shall not be used on an Aircraft without consent from the crew.

2.13. Additional Notes

In general, contact between the patient's skin and the Altius Programmer wand should be avoided due to risk of cross-contamination. Programmer wand should always be separated from the patient's skin with their clothing, or sheet or drape.

WARNING: Risk of Asphyxiation. The Altius System utilizes several cables for power or data transfer. Ensure that you never wrap any of these around your neck to reduce the risk of strangulation or restriction of your airways. Be sure to keep these cables away from young children, or to be aware of what they are doing when in the same room. When not using or charging the Programmer System, ensure that all cables are wound and stored securely.

NOTE: The Altius Programmer System does not contain any user serviceable parts.

WARNING: DO NOT discard the Altius Programmer wand in the trash. The Altius programmer contains electrical non-RoHS components. If disposal is necessary properly consult local environmental laws and regulations governing the disposal of such material.

CAUTION: At this time the Altius PAPC is not intended to be connected to a network, either an internal hospital network or a public network. Doing so is a cybersecurity risk and not recommended.

The Altius PAPC is classified as Class II equipment when connected to the supply mains, Internally Powered ME equipment when the laptop power supply is not connected to mains.

The PAPC is powered by an AC/DC power supply rated at 100-240VAC, 50/60Hz with a maximum output of 65W. The PAPC may have several different power connectors depending on the model. The PAPC's are all rated for power input of 20VDC and 3.25A, for a maximum power of 65W.

The Programmer Wand is classified as a Type BF applied part. The Programmer Wand is a USB powered device with a rating of 5VDC, and 0.5A.

2.14. Cautions and Warnings

The following discussion on potential hazards from the environment focuses on maintaining the utmost patient safety. Although the Altius System IPG was designed to provide the highest possible protection against such hazards, complete immunity against these risks cannot be guaranteed.

For further information check the Prescriber Manual (LB-0195)

2.14.1. Implanted components and MRI scans

WARNING: Safety of MRI/NMRI with an implanted Altius System has not been evaluated. Patients implanted with the Altius System, or any of its components, should not be subject to MRI/NMRI. MRI exposure may result in dislodgement of the Altius IPG or Cuff Electrode(s), heating of the Altius IPG, injury to the nerve, and increased voltage through the Cuff Electrodes or Altius IPG. If MRI/NMRI is needed for any reason, the Altius System must be explanted prior to the diagnostic MRI/NMRI. For patients implanted with the Altius IPG, receiving an MRI/NMRI diagnostic scan, without first explanting the IPG may result in severe patient injury, death or device malfunction.

2.14.2. Electromagnetic Interference

The Altius IPG, and Accessories can be affected by interference from magnetic, electrical, and electromagnetic signals, provided these are sufficiently strong. Most interference will lead to inhibition of communication with the IPG by the patient controller, the Battery Charger or the Programmer System. In rare cases, an interfering signal could trigger inappropriate therapy signal delivery. In addition, interfering signals exceeding a certain threshold may couple enough energy into the IPG to damage the IPG circuits and/or the abdominal tissue and/or in the vicinity of the Cuff Electrode. In other rare cases during a programming visit, incorrect parameter values may be programmed to the IPG from the programmer system.

The patient manual (LB-0196) also covers these factors, and these risks should be disclosed in the discussion with the patient. The susceptibility of a particular device is dependent on the location of the IPG pocket, the type of interfering signal, and on the programmed therapy parameters. Because of the diversity of the potential causes of electromagnetic interference, Neuros Medical cannot characterize and describe all sources of interference and their effects in this manual.

The Altius System IPG contains a magnetic reed switch which may be used in case of emergency to turn off therapy in order to defibrillate the patient. This may inadvertently stop therapy when around strong magnetic sources such as MRI/NMRI, electrical lines, electric motors, electric generators, transformers, strong handheld magnets, and arc welders if held too close to the IPG.

WARNING: Patients should be instructed to be cautious in the vicinity of equipment that generates electrical or electromagnetic fields and to seek medical advice before entering an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.

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 Altius System, including cables specified by Neuros Medical. Otherwise, degradation of the performance of this equipment could result.

WARNING: Use of the Altius System adjacent to or stacked with other equipment should be avoided because it may result in improper operation. If such use is necessary, the Altius IPG and its accessories, and the other equipment it is used next to should be observed to verify that they are operating normally.

This note applies to the Programmer Wand of the Altius System:

NOTE: The EMISSIONS characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

2.14.3. Surgical Cautions and Warnings

For a list of surgical cautions and warnings, see Prescriber Manual (LB-0195), and Implant Manual (LB-0198).

3. Altius Programmer Software Overview

NOTE: Please contact Neuros Medical with any questions, concerns, or issues at 1-833-240-4462.

The Altius Programmer Software contains the commands that are used to read and modify the parameters that control the settings of the Altius IPG.

3.1. Altius Programmer Start-up

After having followed the steps to setup the hardware of the Programmer system in section 2.4 Interconnecting the Programmer components, follow these steps to start the software:

1. Turn on the Altius PAPC.
2. Login to Altius user with the appropriate credentials.
3. Start the Altius Programmer Application by doubling clicking on the Altius icon on the desktop.

Once the Altius Programmer Application has started you will see this screen:

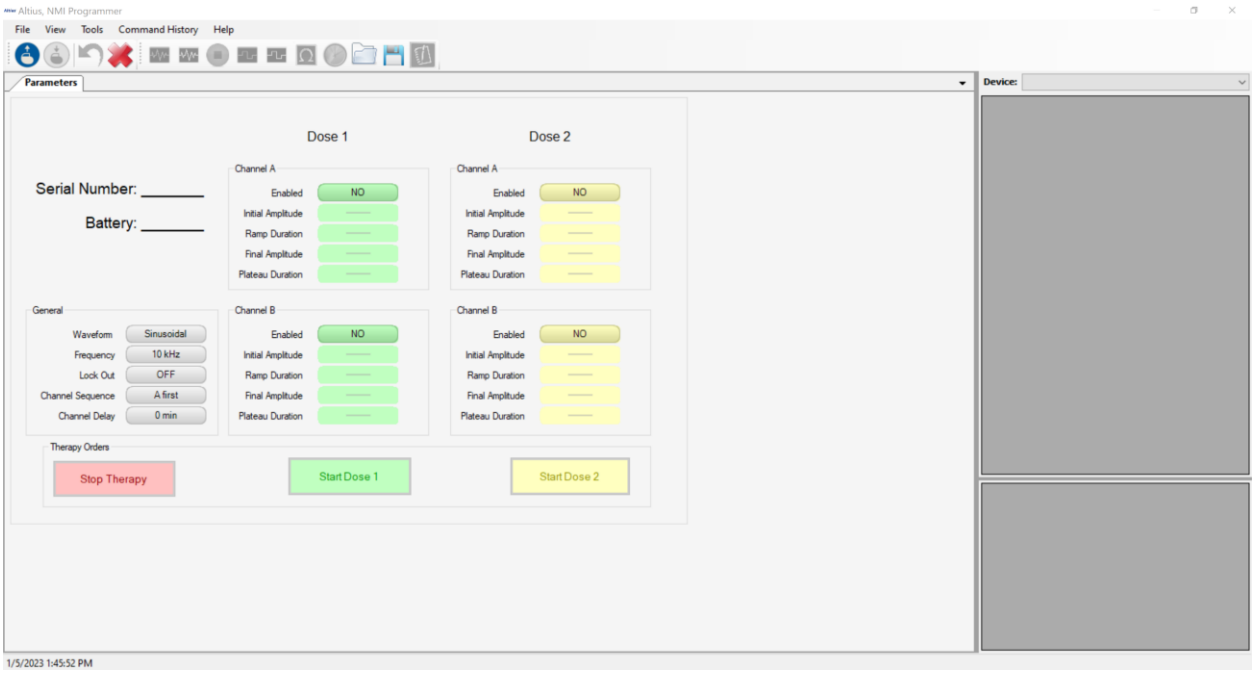


Figure 4: Altius Programmer on Initial Start

NOTE: The toolbar is grayed out except for the **Interrogate** and **Cancel** commands for now.

NOTE: If the Altius Programmer Wand is not connected to the PAPC prior to starting the Altius Programmer software, an error message will display.

Figure 5: Error Message

3.2. Basic Operation of the Altius Programmer Application

Once the Altius Programmer Application has been started, this offers various commands for communicating, interrogating, and programming the Altius IPG.

3.2.1. Communicating with the Altius IPG

The Clinical user can obtain data from the Altius IPG by means of the Programmer wand, which must be placed over the patient's implant site.

Caution: The Programmer wand should be thoroughly cleaned between uses and draped, when necessary to prevent patient skin irritation or contamination.

3.2.2. Interrogation and Programming

The Altius IPG has a set of parameters that control the therapy doses available to the patient. These values are referred to as the *device (therapy/dose) values (parameters)*.

The Altius Programmer Software can read the device values by means of the **Interrogate (Get Parameters)** command. This must be the first action carried out by the physician/clinical user in order to access the data from Altius PG. If the interrogation process is successful, the device values are loaded and displayed on the screen of the Altius Programmer. The values displayed on the screen may be referred to as the parameter values.

The clinical user can review and modify the parameter values using the Altius Programmer. The modified parameter values can then be transmitted to the Altius IPG by means of the **Set Parameters (Program)** command.

Note: The modified Parameter values displayed on the programmer screen are NOT set on the IPG until the **Set Parameters** command is sent.

The **Undo (Set Previous Parameters)** command may be used to revert the device values to those previously programmed.

The **Urgent Programming** command programs the Altius IPG with standard safe parameter values (All Channels Disabled). The **Urgent Programming** command may be initiated by clicking the **Urgent Programming** in the Tools drop down menu or pressing the **Urgent Programming** button on the Altius Programming Wand.

Useful parameter combinations can be stored as ***basic*** files (may also be referred to as "user presets"). The file extension for these are ".mip". After the creation of a particular basic file, the basic file can be loaded for patients who may use similar set of programmed values.

The **Save** and **Load** commands of the Altius Programmer software read and write data to and from the basic (.mip) files. As such the Altius Programmer software can also be used as an editor of the basic files (See Section 16).

3.2.3. Monitoring Tools

The Altius Programmer system can be used to review the commands sent to the Altius IPG during programming and review the Altius IPG log file.

- The Altius Programmer software keeps a log (Command History) of all the interactions with the Altius IPG.
- The Altius IPG keeps a log (record) of all the events and conditions that have occurred. These records can be downloaded from the Altius IPG to the Altius Programmer system.
- The Altius Programmer software can be used to measure the impedance of the cuff electrode(s) (see Section 6).

3.2.4. Closing the Altius Programmer Application

To exit the Altius Programmer Application use of these two ways:

1. Clicking the "X" in the top right corner of the Altius Programmer software screen.
2. Go to the Menu bar, selecting File, in the drop-down menu click exit.

4. Altius Programmer Software Description

The Altius Programmer Software once started and has successfully interrogated the Altius IPG will show the toolbar no longer grayed out and will show the current parameter values of the Altius IPG.

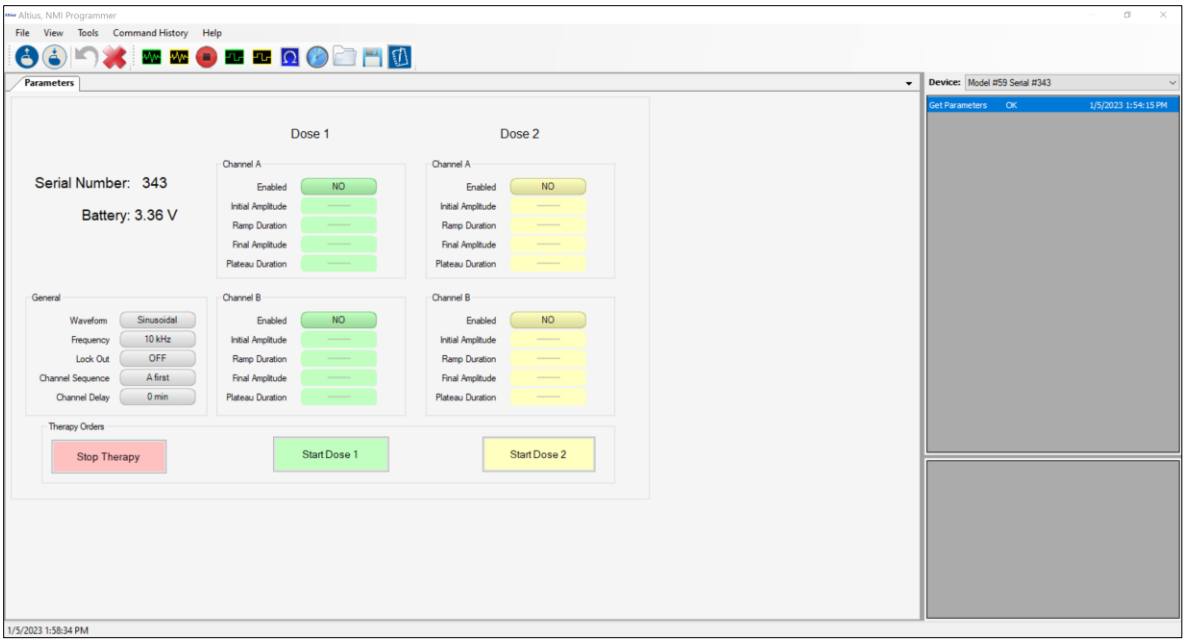


Figure 6: Altius Programmer Software after interrogating an Altius IPG

4.1. Menu Bar

The Altius Menu Bar has five (5) menus with drop down options File, View, Tools, Command History, and Help.

These next few sections may not describe what each function does and is only intended to show where the various functions are.

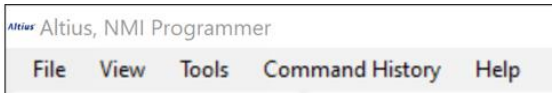
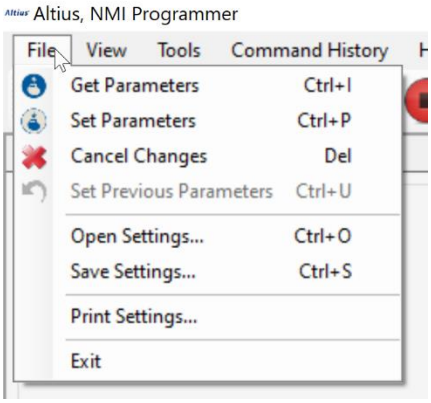


Figure 7: Altius Programmer Software Menu Bar

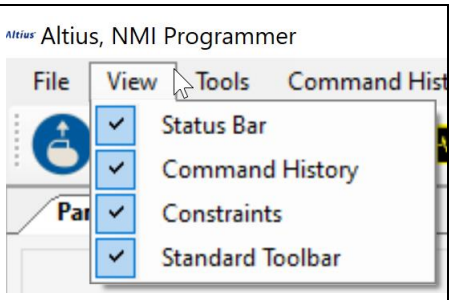
4.1.1. File Menu

The File Menu dropdown allows the use to execute the following functions:

• Get Parameters • Set Parameters • Cancel Changes • Set Previous Parameters • Open (Load) Settings – Base Files • Save Settings – Base Files • Print Settings • Exit	

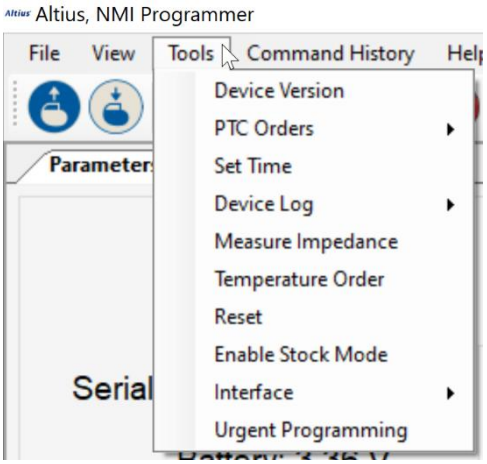
4.1.2. View Menu

The View Menu allows the user to hide/show the Status Bar, Command History, Constraints, and the Standard Toolbar

• The Status Bar is located at the bottom of the screen and at a minimum shows the date and time of PAPC. • The Command History is located in the top right side of the screen and will display the Command History of the Altius IPG. • The Constraints view is located in the right side of the screen under the Command History. • The Standard Toolbar is located on the main toolbar line and consists of the following functions: Get Parameters, Set Parameters, Set Previous Parameters, and Cancel Changes.	

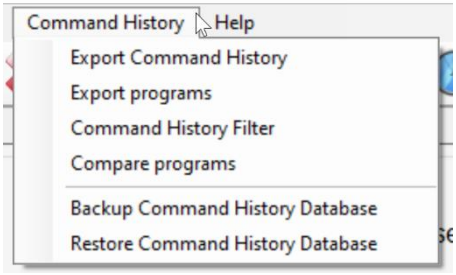
4.1.3. Tools Menu

The tools menu contains the following set of Commands:

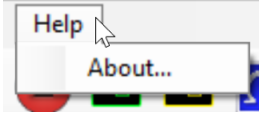
• **Device Version** command • PTC Orders – Contains the button commands on the Altius Patient Controller • **Set Time** command • Device Log – Contains the **Clear Device log** and **Read Device Log** commands • **Measure Impedance** command • **Temperature Order** command • **Reset** command • **Enable Stock Mode** command • Interface – Shows the Interface Version information • **Urgent Programming** command	

4.1.4. Command History Menu

The Command History menu contains the following set of commands:

• **Export Command History** • **Export programs** • **Command History Filter** • **Compare Programs** • **Backup Command History Database** • **Restore Command History Database**	

4.1.5. Help Menu

The Help Menu contains the **About** command. This will display the Altius Programmer Software files and their version information.	

4.2. Toolbar

The Toolbar of the Altius Programmer contains some of the most common commands used in the Altius Programmer.

The List of Symbols and commands from left to right are:

• Get Parameters (Interrogate) • Set Parameters • Set Previous Parameters • Cancel Changes • Start Dose 1 • Start Dose 2 • Stop Therapy • Single Pulse Dose 1 • Single Pulse Dose 2 • Measure Impedance • Set Time • Load Settings • Save Settings • Read Device Log	

4.3. Parameters tab

The parameters tab of the Altius Programmer Software shows the device settings, Serial number of the Altius IPG, and the Battery voltage of the Altius IPG. This tab also has the following command buttons at the bottom of the screen: Stop Therapy, Start Dose 1, Start Dose 2.

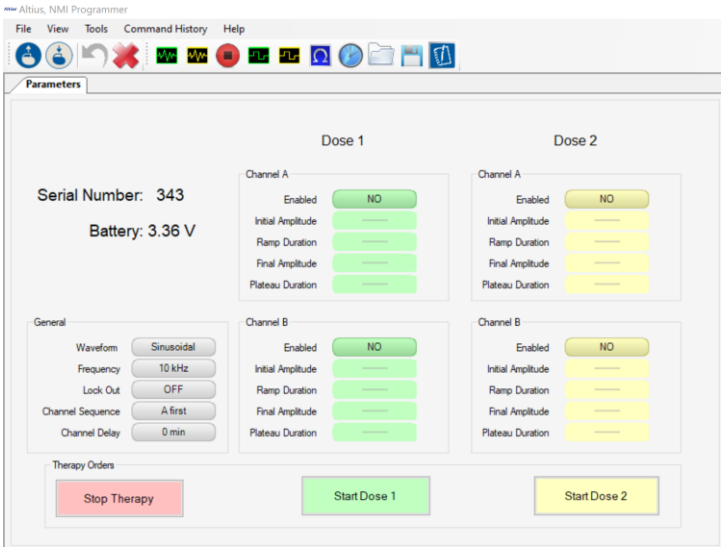


Figure 8: Default Parameters in the Altius Programmer Parameters Tab

4.4. Altius Parameter Settings

The Altius IPG can be programmed by the Altius Programmer Application with the following set of values for clinical use:

Altius IPG Parameter Ranges		
General Parameters	**Specifications**	**Increment**
Waveform	Sinusoidal	-
Frequency (High)	5khz, 10khz	-
Channel Sequence	A First, B First	-
Lockout	0.5hr	-
Channel Delay	0 min	-
Dose/Channel Parameters	**Specifications**	**Increment**
Enabled	Yes/No	-
Initial Amplitude	0-8Vp	0.1V
Ramp Duration	0-15 min	1 min
Final Amplitude	0-16Vp	0.1V
Plateau Duration	0-30 min	1 min

Table 1: Altius IPG Parameter Ranges

At the Patient's initial activation and programming visit, to find the patient's response to Direct Electrical Nerve Stimulation their parameter settings will be determined using a 15-minute Ramp Duration which will involve the voltage will start at 0Vp and over the 15 minutes be increased to 15Vp. Using the patient's responses the parameters will then be set to achieve a sensation that is strong, but tolerable transient sensation for the patient.

Subsequent adjustment visits will be made based on the patient's ability to handle the therapy with either an increase or decrease of that therapy.

4.5. Altius IPG Parameter Tab Information

The Altius IPG Serial Number displayed in the Parameters tab is a unique number to the specific device.

Battery Voltage displayed in the Parameters tab shows the current voltage of the Altius IPG. This voltage can be used to infer how well charged the implanted device is. If the Altius IPG is below 3.3 volts, it will have to be charged prior to interrogating and programming. A full charge is at approximately 4.10 volts. For more information on the IPG battery and charging see the Altius Clinician Guide (LB-0195)

5. Interrogation

5.1. Communicating with the implanted Altius IPG

After having followed the steps in section 3.1, place the Altius Programming Wand over the implant site, at a distance of no more than 3.5cm (1.4 in) from the Implanted Altius IPG. A blinking green or yellow light on the signal strength indicator indicates that the IPG is within communications range of the Programmer Wand. A blinking red light indicates that the distance is excessive, and communications may be difficult, but not impossible. No light at all means that the Programmer Wand and Altius IPG are out of communication range or that the battery of the Altius IPG is discharged below the minimum charge for communication, and thus incapable of communicating with the Programmer Wand.

5.2. Interrogating the Altius IPG

To read the parameters of the Altius IPG:

1. Ensure that the Programming Wand is placed over the implant site and there is a green or yellow blinking light.
2. Interrogate the Altius IPG using one of the three options:
    a. Select **Interrogate** (**Get Parameters**) button on the toolbar
    b. Select File then Select **Interrogate** (**Get Parameters**) button on the toolbar
    c. Press the Keyboard shortcut <**Ctr+I**>
    d. Press the **Interrogate** (**Get Parameters**) button on the Programming Wand

If the Interrogation is successful, the Altius Programmer Application will display the message "Get Parameters OK" in the Command History

The IPG Model, Serial Number, Battery Voltage, and Therapy parameters will appear on screen. Also, any previous Command History will be displayed on the right side of the screen.

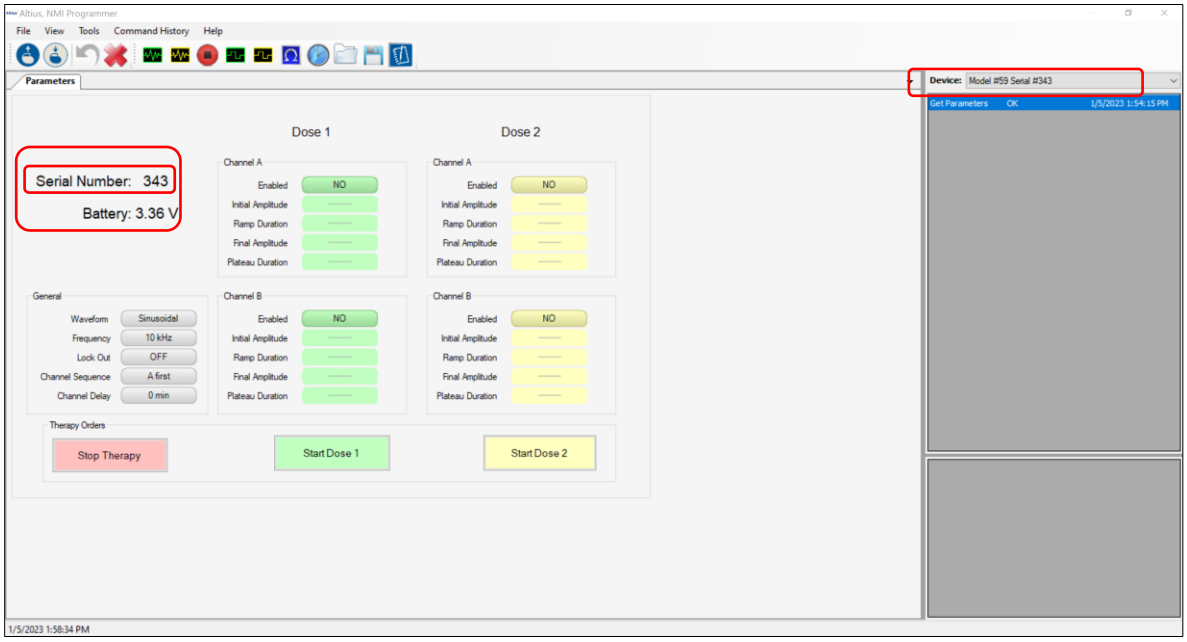


Figure 9: IPG Model, Serial Number and Battery Version

However, if the Programmer Wand is not well positioned or is moved out of position the **Get Parameters** may fail and the Programmer Application will display the "Get Parameters error" in the Command History and a pop-up window will show:

Figure 10: Get Parameters Error Message

If this error occurs, they can close the error window, and ensure that the Programmer wand is in the correct position and attempt **Get Parameters** again following the steps above.

6. Measuring Cuff Electrode Impedance

The impedance of the Cuff Electrode(s) is used as an integrity check. The Impedance check is essential to ensure the device is both connected and working properly. If the impedance measurement results in unusual readings, it could indicate an issue with the device continuity.

The Impedance for a Cuff Electrode will have a natural variability based on each patient and size of Cuff Electrode used.

The Altius Programmer Application will display 4 distinct Impedance ranges:

- >180 Ω
- 180 Ω – 3,000 Ω
    - This is the only range where a number will be given.
    - The accuracy of this range is 10%.
- > 3,000 Ω
    - Indicates a range 3,000 – 20,000 Ω
- High Impedance
    - Indicates a range of 20,000Ω or greater

The typical expected range is:

Nerve Diameter (mm)		≤ 5	6 – 8	9 ≤
Cuff Size		Small	Medium	Large
Impedance Ω	Good	500 – 1400	200 – 800	
	OK	180 – 2000	180 – 1200	
	Bad	< 180 or > 2000	< 180 or > 1200	

Table 2: Impedance Range

NOTE: If impedance measurements are outside of these ranges, check with the patient to determine if they are still feeling the therapy. If they are not feeling therapy, then something may be wrong and further troubleshooting may be required.

To Measure Impedance:

1. Place (or replace, if necessary) the Programmer Wand over the Altius IPG.
2. To get the Impedance:
    a. Press the **Measure Impedance** button on the toolbar.
    b. Select Tools on the menu bar and then select **Measure Impedance.**
3. View the Impedance values and compare them to the Impedance Values above and determine if any additional action is required.

Figure 11: Impedance Measurement pop-up Window, Channel A only

4. Once done reviewing the measurement values, close the window.

    NOTE: The Impedance Measurement Values are stored in the Command History.

5. To repeat, follow steps 1-4.

7. Single Pulse Testing

Single Pulse is used as another device integrity check. This test ensures that the Altius IPG and Cuff Electrode(s) are working properly, and that the patient can feel the pulse. If the Single pulse results in an unusual result it could indicate an issue with the device continuity. The single pulse used is a biphasic 100 µs pulse width.

Single Pulse Dose 1 and **Single Pulse Dose 2** execute the Single Pulse based on the Final Amplitude Parameter for Channel A and/or Channel B.

Warning: The Single Pulse Dose 1 and Dose 2 commands will send a Single Pulse of energy to both Channel A and Channel B at the Final Amplitude voltage, if both are enabled. It is strongly recommended that when using Single Pulse, the test is only executed on one channel at a time.

The steps to execute the Single Pulse Dose 1 or Dose 2 are:

1. Ensure that the programming wand is in place.
2. Set the Dose and Channel Final Amplitude to the value to be tested.
3. Disable the Channel that the Single Pulse test is not being used for.

4. **Set Parameters** by one of the following methods:
    a. Click the **Set Parameters** button on the toolbar

b. Go to File menu and select **Set Parameters**

c. Press the keyboard shortcut <Ctrl+P>

d. Press the **Set Parameters** button on the Programming Wand

5. Check that the Parameters were set in the Command History
6. Click the Single Pulse Dose button being tested.
7. To repeat this process, follow steps 1-6.

8. Setting the Clocks on the Altius IPG and Altius PAPC

The PAPC and the Altius IPG are not connected to any networks for cybersecurity reasons. The clocks on both devices will drift from the current time, so they should be regularly reset. The PAPC clock should reset to the current time, or a standard time zone. The IPG can get its time from the PAPC, but a manual time may also be entered.

The time on the PAPC and the IPG are used to log the events as they occur on the Programmer Application in the Command History and on the Altius IPG in the Log File.

8.1. Setting the PAPC Clock

The PAPC runs Windows 10. To reset the clock, follow these steps:

1. Start the PAPC.
2. Login to the PAPC.
3. Right Click on the lower left of the screen where the time and date are.
4. Click on the Adjust Time/Date, this will open a settings window for Date & Time.
5. Click on the Change button under the Set the Date and Time Manually.
6. Enter the current Date and Time.
7. Close the settings window.

8.2. Setting the Altius IPG Clock

To reset the clock on the Altius IPG follow these steps once the Programmer Application is running and **Get Parameters** has successfully retrieved the parameters from the IPG:

1. To start Select Time by:
   a. Clicking the **Set Time** button on the toolbar.
   b. Going to Tools menu and clicking **Set Time.**

2. A pop-up window will display the Current Device Time and the Current PC Time.

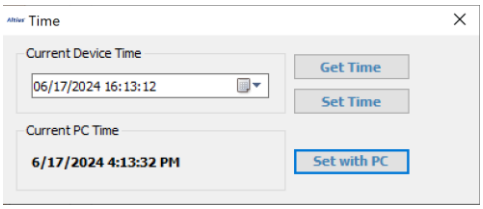


Figure 12: Neuros Altius IPG Clock Window

3. Setting IPG Time
   a. If the PAPC has already been reset, Click the **Set with PC** button.
   b. If setting the time manually, enter the desired current device time. The format followed is MM/DD/YYYY HH:MM:SS, then click **Set Time**.

      NOTE: MM is the two digit number for the Month, DD is the two digit day of the month, YYYY is the four digit year, HH is the hour expressed in 24 hours, MM is the two digit minute, SS is the two digit second.

4. Once the IPG time is set, click the **Get Time** button to get the latest Altius IPG time.
5. Compare this time to the current PAPC time displayed.

9. Modifying and Setting Parameter Values

Modifying and Setting Parameter Values should always be based on patient feedback.

To use the Programmer Application Software to Modify and set Parameter values follow the steps below, ensuring that the Programmer Application is running, and **Get Parameters** has successfully retrieved the parameters from the IPG.

CAUTION: Ensure that the parameters set are appropriate to the patient prior to programming.

NOTE: All Parameter Values are modified by clicking the value to be modified, which will open the value window for the specific parameter.

WARNING: Use of any non-clinical setting has not been tested or proven to work to reduce pain for the intended use with the patient population.

1. Select the General Parameter Value to be modified:
   a. Waveform
      i. Waveform is the shape of the wave used for the therapy.
      ii. Sinusoidal is the clinical value to be used, any other value used for Waveform is considered non-clinical.
   b. Frequency
      i. Frequency is the setting which selects the electrical frequency used to deliver the therapy voltage.
      ii. 5kHz and 10kHz are the Clinical values to be used, any other value used for Frequency is considered non-clinical.

c. Lockout
    i. Lockout is the amount of the patient is unable to begin another therapy session
    ii. 30 min is the minimum recommended lock-out time.
    iii. Off should be used only when programming therapy in the clinic.
d. Channel Sequence:
    i. Channel Sequence is the sequence for which Channel goes first.
    ii. A first is the default value, B first is also valid if determined by the clinician
e. Channel Delay
    i. Channel Delay will delay the start of the second channel, if A first is selected for Channel sequence, Channel B will start after Channel A completed its ramp time and reached its plateau voltage. If Channel Delay is set to 0 min, then the second channel will begin immediately following the first channel completing its ramp time.
    ii. Channel Delay value of 0 is the default value.

2. Modifying and Setting Dose 1 & Dose 2, Channel A & Channel B Parameter Values:
    a. Enabled
        i. Yes – The rest of the Parameters are available for programming
        ii. No – The Parameter programming is disabled for the rest of the parameters.
    b. Initial Amplitude
        i. Initial Amplitude is the voltage that Dose 1 Channel A will start at.
        ii. This value can be set from 0 to 8 Volts and an increment of 0.1 Volts.
        iii. This value must be equal to or less than the Final Amplitude Voltage Parameter Value.
    c. Ramp Duration
        i. Ramp duration is the amount of time that the voltage will ramp up until it reaches the final amplitude voltage.
        ii. This value can be set from 0 to 30 mins, with increments of 1 min.
    d. Final Amplitude
        i. Final Amplitude is the voltage amplitude reached once the Ramp has completed.
        ii. This value can be set from 0 to 16 volts, with increments of 0.1 volts.
        iii. This value must be equal to or greater than the Initial Amplitude Parameter Value.
    e. Plateau Duration
        i. Plateau Duration is the amount of time that the Final Amplitude Voltage runs.
        ii. Plateau Duration can be set from 0 minutes to 60 minutes with an increment of 1 minute.

3. If any values appear in Red text this indicates that two parameter values conflict with each other, and that one of the values needs to be corrected.
    a. In addition to appearing in red, the conflict will appear in the conflict window in the lower right-hand corner of the Programmer Application.
4. Ensure that the Programming wand is placed over the implanted IPG.
5. Once all conflicts have been resolved, all changed parameter values should appear in Blue text. Select the **Set Parameters** command.
6. The Programmer Application will send the new parameters to the IPG, and the "Set parameters Ok" will appear in the Command History Window.

10. Starting and Stopping Therapy Session with the Programmer System

To ensure that the programmed parameter values are acceptable for the patient to use, it is important that the settings be run in the clinical setting. The following instructions assume that the Programmer Application has been started, and Programmer wand is in place over the IPG, and that any parameters that need to be modified have been, per Section 9.

Caution: When starting a therapy session in Clinic, it is important to remind the subject to keep the Programmer Wand in place over the Implanted IPG in the event that the therapy needs to be quickly stopped.

10.1. Starting Therapy Session

1. Check to ensure that the Programmer is in place over the Altius IPG.
2. Check to ensure that the desired Parameter Values have been sent to the IPG by using the **Get Parameters** command.
    a. Correct any values. Refer to Section 9.
3. Start the therapy session by executing the **Start Dose 1** or **Start Dose 2** command by one of the following ways:
    a. Click the start **Dose 1** or **Start Dose 2** green or yellow buttons under the respective Dose 1 or Dose 2 Parameter Value sets.
    b. Click the start **Dose 1** or **Start Dose 2** green or yellow symbols on the Toolbar.
    c. Click Tools on the menu bar, click the PTC orders menu, and Select **Start Dose 1** or **Start Dose 2**
4. The order will then be transmitted to the device and the Start Dose 1 OK or Start Dose 2 OK will appear in the Command History.

10.2. Reading Device Log File

1. Ensure that the Programmer Wand is in place over the implanted Altius IPG.
2. Stop the therapy by executing the **Stop Therapy** command by one of the following
    a. Click the **Stop Therapy** button under the therapy orders section
    b. Click the icon for **Stop Therapy** on the toolbar.
    c. Click Tools on the menu bar, click the PTC orders menu, and Select **Stop Therapy**
3. The order will then be sent to the Altius IPG and Stop Therapy Ok will appear in the command history.

11. Device Log File

The Device Log file can be a useful tool to assess changes in programming, frequency in charging, or the frequency in device use among other uses.

11.1. Reading Device Log File

To Read the Device Log file from the IPG follow these steps, assuming the Programmer Application has been started and the programmer wand is in place:

1. Ensure that the programmer wand is in place over the IPG.
2. Execute the **Read Device Log** command by one of the following methods:
    a. On the toolbar select **Read Device Log** icon
    b. On the menu bar select Tools, in the drop down menu select Device Log, and Select **Read Device Log**
3. The Device log will open in a Pop-up window displaying the most recent event in the log that will appear first and with the oldest event appearing last.

NOTE: The IPG log has a limited memory and will only be able to store a minimum of 300 events and the date and time they occurred according to the IPGs on board clock.

11.2. Device Log File storage and Data

An event can be described as any external command the IPG is given, or any internal event recorded for its safe operation, such as:

- Starting or ending therapy
- Starting a charging session including recording temperature values
- Receiving new parameter values
- Starting and ending the lock out period

The Device Log, once downloaded onto the PAPC is stored in the following directory:

C:\Neuros Altius Programmer X.X.X.X\Log

Where X.X.X.X is the version of the Altius Programmer Application i.e version 1.1.0.0.

The device log file names follow the naming convention “LogFile_<IPGSN>”, where IPGSN is the serial number of the IPG.

The Device log is stored as a .csv file and can be accessed by opening it notepad or Microsoft excel. It is strongly recommended to copy the log file to an external USB drive and review it on a different computer.

If the same IPG and PAPC are used throughout a patient’s set of programming visits, the log file stored on the PAPC will be updated with the new data from the IPG in the order from oldest data to newest data.

11.3. Clearing Device Log

The Device log can also be cleared.

WARNING: Clearing the Device Log if it has not been downloaded onto the PAPC means that data is no longer available and is irrecoverable.

Follow these steps to clear the Device log:

1. Ensure that the programmer wand is in place over the IPG.
2. On the menu bar select Tools, in the drop down menu select Device Log, and Select Clear Device Log
3. The Clear Device Log OK will appear in the command History

12. Command History

The Command History stores the list of commands that the PAPC sends to a specific Altius IPG. It is displayed in the middle right hand corner of the screen.

12.1. Saving and Exporting the Command History

The Command History can be backed up and exported by following these steps:

1. Open the Programmer Application
2. On the Command History Box on the right side of the screen select the IPG Serial Number of Interest from the Drop down, if the IPG has not already been selected.
3. On the Menu Bar select Command History, select Export Command History

   This will bring up a File Save box for the default file location which is C:\Neuros Altius Programmer X.X.X.X\Log. Enter the name of the file you would like to save the Command History as. Where X.X.X.X is the version of the Altius Programmer Application i.e version 1.1.0.0.

   NOTE: The recommended file format to use is CmdHist_<IPGSN>, where IPGSN is the serial number of the IPG. Variations to include date, and the clinician performing the programming are encouraged.
4. Save the file.

The Command History File will be saved as a .txt file. It is recommended to transfer the file via USB jump drive to another computer.

12.2. Compare Programs

Compare Programs can be accessed by going to the Menu Bar and selecting Command History. In the Command History menu, select Compare Programs.

This will open a screen that will show the Get Parameter and Set Parameter Values sent to an Altius IPG. Once the Window is open, double click a Set Parameter command other than the latest one, and it will show the parameter values that are different between the current programmed parameters values and the parameter values from the selected Set parameters command. If nothing shows up, then there is no difference between the two parameter value sets.

The Window also shows a button with **First of Today**. This button will show the first programmed command of the day.

The **Print** Button will open a print window where it can be saved.

Once done, click the **x** button in the top right corner of the screen, or click the **Close** button on the bottom right of the screen.

12.3. Export Programs

The export Program command can be used to export all the Set/Get parameter commands with all programmed parameters in the current IPG log information on the PAPC.

To Export Programs, go to the menu bar, select Command History, Select Export programs. This will open a dialog box to save the file as .txt. The file will be saved in the C:\Neuros Altius Programmer .X.X.X\Log folder.

Where X.X.X.X is the version of the Altius Programmer Application i.e version 1.1.0.0.

12.4. Command History Filter

CAUTION: Changing the Command History Filter may inadvertently hide useful information about the list of commands sent to the IPG from the PAPC.

The Command History Filter may be accessed by going to the Menu Bar, selecting Command History, and clicking on Command History filter. This will open a window where the commands shown in the Command History Window can be filtered in or out.

12.5. Backup/Restore the Command History File Database

WARNING: Exporting or Importing the Command History File Database should only be done at the direction of Neuros Medical personnel.

If a Backup Command History Database or Restore Command History Database needs to be done, it should be executed by Neuros Medical personnel, or under their supervision.

13. Urgent Programming

Urgent programming will set the IPG to the default settings of Doses and Channels disabled.

CAUTION: Urgent Programming will clear the current programmed parameter values when executed.

To use Urgent programming:

1. Ensure that the Altius Programmer Application has executed the **Get Parameters** command successfully.
2. With the Programmer Wand still over the Altius IPG, execute **Urgent Programming** by one of the following methods:
    a. Clicking the **Urgent programming** button on the Programming Wand
    b. Going to the menu bar, selecting Tools, and clicking on **Urgent Programming**

14. Resetting the Altius IPG

The Altius IPG is designed to protect itself if an internal fault occurs by going into a safe mode (down mode), where all therapy is disabled, and the ability to turn on therapy from the Programmer Application, or the Patient controller is disabled until the IPG is Reset. The IPG will go into Safe Mode if it detects an internal fault, or if it is exposed to certain conditions such as, but not limited to electrocautery or defibrillation, or strong magnetic fields that trigger safe mode.

If the Altius IPG goes into safe mode the patient will know if they attempt to activate Dose 1 or Dose 2, or to charge the Altius IPG, the Patient Controller and the Battery charger will activate

the Contact Physician light. The patient must come in for a programming visit to reset the Altius IPG and reactivate therapy.

To Reset the IPG:

1. Interrogate the Altius IPG with Programming Wand positioned over the implant site
2. An error screen will come up stating that the IPG is in down mode.
3. On the Menu Bar select Tools
4. In Tools, click **Reset**
5. The Reset will order will be sent to the IPG, and the IPG will reset itself to the default settings of Dose 1 & 2, Channels A & B off, the Reset OK will appear in the Command History.
6. If executed and the default settings appear the reset was successful, the user parameter values may now be modified to the patient's previously programmed values or modified if desired by the patient.

CAUTION: If This does not work, the clinician should contact Neuros and have Neuros field staff see the patient.

15. Magnet Mode

The Altius IPG contains a magnet activated reed switch in case of emergency where the therapy needs to be turned off.

If a Magnet with a strength of 10 to 25 gauss is used close to the Implanted location of the IPG, a Dose disabled by magnet event will be logged by the IPG, and if therapy is active, the dose will be disabled, and the lockout period will begin.

16. Using Base Files

Base files may also be referred to as Settings or Setting Files. They are stored as .mips files. A base file may be used to save or load common starting parameter values.

The default file storage location for Base/Settings file is C:\Neuros Altius Programmer X.X.X.X\Log folder

Where X.X.X.X is the version of the Altius Programmer Application i.e version 1.1.0.0.

16.1. Save Base File

To Save a Base/Settings file:

1. Open the Programmer Application
2. Change the Parameters to the desired value, ensure that show up in Blue text
3. Save the Base/Settings file by one of the following methods:
    a. Click the **Save Settings** Button on the Toolbar
    b. On the Menu Bar go to File, and in the dropdown, Click **Save Settings**
    c. Use the Keyboard command <Ctrl+s>
4. This will open the save file window, enter the name for the file, and click Save.

16.2. Load Base file

To Load a Base/Settings file:

1. Open the Programmer Application
2. Ensure that the Programmer Wand is placed over the IPG.
3. Execute the **Get Parameters** command
4. Load the Base/Settings file by one of the following methods:
    a. Click **Load Settings** button on the Toolbar
    b. On the Menu Bar go to File, and in the dropdown menu, Click **Load Settings**
    c. Use the Keyboard command <Ctrl+0>
5. This will open the Open Settings file window, select the file to load, and click Open, or double click on the file name.
6. The file is now loaded, and the parameter differences will appear in Blue text

17. Print Settings

The Print Settings function allows the user to Print the Settings currently displayed to an Adobe pdf file.

To use Print Settings:

1. Go to the Menu Bar, select File, Click **Print Settings**
2. This will open a Print preview window, with the Adobe pdf symbol will be displayed in the top right of the screen.

WARNING: It is not recommended to attempt to connect the Programmer Application PC to an external Printer.

3. Once the file has been saved it may be transferred to a USB jump drive for review off of the PAPC.

18. Device Temperature

The **Temperature Order** command will have the Altius IPG communicate the temperature of the IPG in degrees Celsius.

To execute the **Temperature Order** command, follow these steps:

1. Ensure that the Programmer Application has been started, and that the Programmer Wand is in place over the Implanted Altius IPG.
2. Execute the **Get Parameters** command.
3. Go to the Menu Bar, select Tools, in the drop-down menu click **Temperature Order**.
4. If executed correctly, the Temperature will display in a pop-up window.

Get Temperature OK will appear in the Command History Window.

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

Appendix I: Replaceable Parts & Cables

The Altius System is fully replaceable, there are no User serviceable parts.

For replacement of any part of the Altius System please contact your Neuros Medical Representative.

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

Non-Implantable replaceable Components:

Neuros Medical Part Name	Expected Service Life	Neuros Medical Part Number	Cable Length (If Applicable)
Altius Patient Controller	5 Years	FG-604-000	N/A
Altius Battery Charger	5 Years	FG-603-000	61cm (24in) (Charger to Paddle)
AC Adapter for Altius Battery Charger	5 Years	PC-200-044	170cm (66 in)
Altius Programmer Wand	5 Years	FG-606-000	305cm (10ft)
Programmer Application PC (PAPC)	5 Years	FG-608-000	N/A

Implantable replaceable Components

Neuros Medical Part Name	Neuros Medical Part Number	Cable Length (If Applicable)
Altius IPG*	FG-601-000	N/A
Cuff Electrode Small	FG-600-001	100cm (39 in)
Cuff Electrode Medium	FG-600-002	100cm (39 in)
Cuff Electrode Large	FG-600-003	100cm (39 in)

*The battery in the Altius IPG has undergone simulated bench tests to demonstrate battery longevity at nominal settings and usage is 10 years.

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Appendix II: Wireless Specifications of the Altius System

Communication/Telemetry and Wireless Charging:

Patient Controller and Programming Wand to the IPG(Communication)

- Modulation: ASK (Amplitude Shift Keying)
- The Amplitude is 0 and a 1 is 305µs signal
- Transmit Frequency: 20kHz
- Power: 0.27 Watts (W)

Battery Charger to Altius IPG (Charging)

- Modulation: PWM (Pulse Width Modulation) (Only for limited communication)
- The pulse are 1.07ms for a 0 and 3.36 ms for a 1
- Transmit Frequency (386kHz – 490kHz)
- Transmitter Power is 0.52 W

Altius IPG to the Patient Controller and Programming Wand (Communication)

- Modulation: PPM (Pulse Position Modulation)
- The position between two pulses for a 0 is between 183µs, a 1 is 275µs
- Transmit Frequency: 19kHz
- Power: 1.8 mW

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

Appendix III: Electromagnetic Interference Information

The Altius System can be used in 4 main configurations and used accordingly as listed below:

1) The Battery Charger Being Charged by AC Mains
2) The Battery Charger Being Used to Charge the IPG Battery
3) The Patient Using the Controller to turn the IPG On/Off*
4) The Programmer System Being Used to Program the IPG

*Due to practical limitations of testing, configuration 3 and configuration 4 were determined to be equivalent to each other as the Patient Controller and Programmer Wand use the same circuitry for transmitting and receiving telemetry data.

The Altius System was found to be complaint following the testing listed below for the specified configurations and environments as specified below:

Test Standard	Configuration	Compliance Level	Electromagnetic Environment Guidelines
CISPR 11 Radiated Emissions	1,2,3	Group 1 Class B	The Altius System uses RF energy only for its internal function; therefore, its RF emissions are low and ae not likely to cause any interference in nearby electronic equipment. The Altius IPG, Battery Charger and Patient Controller 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.
CISPR 11 Radiated Emissions	4	Group 1 Class A	The Altius Programmer System is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
CISPR 11 Conducted Emissions	1	Group 1 Class B	The Altius Battery Charger 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.
IEC 61000-3-2 Harmonics	1	Harmonics Class A	
IEC 61000-3-3 Flicker	1	4% max	
IEC 61000-4-2 ESD Immunity	1,2,3,4	±8kV Contact; ±2,4,8,15kV Air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, relative humidity should be 30% or higher. The operator may have to reset the system if the communication between the Programmer Wand and the PAPC is interrupted.
IEC 61000-4-4 EFT Immunity	1	±2kV 100kHz repetition frequency	The Battery Charger 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.
IEC 61000-4-5 Surge Immunity	1	±0.5,1kV Line to Line; ±0.5,1,2kV Line to Ground	

Test Standard	Configuration	Compliance Level	Electromagnetic Environment Guidelines
IEC 61000-4-6 Conducted RF Immunity	1,2,4	3Vrms 0.15 – 80MHz; 6Vrms in ISM and Amateur Radio Bands; 80% 1kHz AM	Portable and mobile RF communications equipment should not be used at levels as tested per the compliance levels listed in the table below.
IEC 61000-4-3 Radiated RF Immunity	1,2,4	10V/m 80MHz – 2.7GHz 80% 1kHz AM	
IEC 61000-4-8 Power Frequency Magnetic Field Immunity	1,2,3,4	30A/m 50/60Hz	The Altius Programmer System is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes. The Altius IPG, Battery Charger and Patient Controller 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.
IEC 61000-4-11 VDI Immunity	1	0% UT for 0.5 Cycle at 0,45,90,135,180,225,270,315 degrees 0% UT for 1 Cycle 70% UT for 30 Cycles 0% UT for 300Cycles	The Battery Charger 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. **Note:** If the user of the Altius Battery Charger requires uninterrupted operation during power mains interruptions, it is recommended to power the Altius Battery Charger from an uninterruptible power supply or battery.
IEC 60601-1-2 ed4.1 Proximity Radiated RF Immunity (Table 9)	1,2,4	See Table 9 Compliance Levels on next page	The separation distance between an interfering RF transmitter and any Altius System Device should be greater than 0.3m (12in) and the maximum power from the RF transmitter should not exceed 2 W or 28V/m at a distance of 0.3m.
IEC 60601-1-2 ed4.1 Proximity Magnetic Field Immunity (Table 11)	1,2,3,4	30kHz CW 8A/m 134.2kHz 2.1kHz PM 65A/m 13.56MHz 50kHz PM 7.5A/m	The separation distance between an interfering magnetic field and the Altius System should be greater than 15cm, unless intentionally activating the magnetic reed switch of the IPG to deactivate therapy.

Compliance Levels from Table 9 of IEC 60601-1-2 ed 4.1

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

ALTIUS SYSTEM IPG PROGRAMMER MANUAL

Appendix IV: Federal Communications Commission (FCC)

The Altius Patient Controller and the Altius IPG:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

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

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

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

The Altius Programmer Wand:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause harmful interference, and

(2) this device must accept any interference received, including interference that may cause undesired operation.

This equipment has been tested and found to comply with the limits for a Class A digital device, pursuant to part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference when the equipment is operated in a commercial environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference in which case the user will be required to correct the interference at his own expense.

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

The Altius Battery Charger:

This Device Complies with Part 18 of the FCC rules.

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.

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

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.

Altius® System Direct Electrical Nerve Stimulation System
Clinical Summary

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

LB-0201 Rev C

ALTIUS SYSTEM CLINICAL SUMMARY

Neuros Medical (USA), Inc
26800 Aliso Viejo Parkway, Suite 250
Aliso Viejo CA 92656, USA
Support Phone Number: 833-240-4462

Please read the complete documentation provided before you use the device.

Although FDA has determined that the probable benefits outweigh the probable risks, there remains some uncertainty regarding the manufacturer's human factors engineering (HFE) and usability engineering (UE) analysis and validation testing. As a condition of approval, FDA is requiring the manufacturer to provide an HFE/UE analysis and validation testing and recommending that this analysis and testing is designed using the FDA's 2016 guidance document "Applying Human Factors and Usability Engineering to Medical Devices"
(https://www.fda.gov/media/80481/download).

This manual can also be found at: www.neurosmedical.com

The Altius® System is protected by several U.S. Patents.
For an up-to date list of relevant patents and patent applications, visit our patents page:
https://www.neurosmedical.com/patents

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Information available for the Altius System:

ALTIUS SYSTEM CLINICAL SUMMARY

The information for prescribers manual and patient manual provide information about indications, contraindications, warnings, precautions, adverse events, sterilization, patient selection, individualization of treatment, and component disposal.

Product manuals, including the patient guide, the programming guide, and implant manual, provide device descriptions, package contents, device specifications, battery longevity and instructions for use.

For information that supports the clinical use of the Altius System, this document includes a clinical summary.

ALTIUS SYSTEM CLINICAL SUMMARY

1. INDICATIONS FOR USE

The Altius® Direct Electrical Nerve Stimulation System is indicated as an aid in the management of chronic intractable phantom and residual lower limb post-amputation pain in adult amputees.

2. SUMMARY OF PRIMARY CLINICAL STUDY

Neuros Medical Inc. performed a pivotal clinical study, the QUEST Study, to establish reasonable assurance of safety and effectiveness of post-amputation pain relief in lower limb adult amputees in the U.S. under IDE #G130203. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

2.1. Study Design

Subjects were treated between 09 October 2014 and 13 September 2021. The last subject completed the Month 3 primary endpoint follow-up on 22 December 2021 and the Month 12 secondary endpoint follow-up on 8 November 2022. The database for this PMA reflected data collected through 4 January 2023, which was the complete dataset through Month 12, and included 180 subjects in the Full Analysis Set (FAS). There were 34 investigational sites, all located in the U.S.

The study was a multi-center, prospective, randomized, double-blinded, active-sham-controlled trial comparing the Altius System (programmed to therapeutic stimulation level, Test) to an active sham (Altius System programmed to deliver low-level sub-therapeutic stimulation, Control).

Subjects and study staff (e.g., investigators, study coordinators, evaluators) were blinded as to their treatment assignment. A total of 180 subjects met all enrollment criteria, were implanted with the Altius System and were randomized at the time of programming in a 1:1 ratio to the Test and Control groups.

- Randomized, controlled study design
    - Randomization post-implant
    - Active sham control
- Blinding/Masking
    - Study subjects
    - Investigators and site personnel performing subject assessments
    - Sponsor
    - Data Monitoring Committee
    - Independent Physician Adjudicator
    - Study Monitors
- Maintained equipoise
    - Balanced interactions with both treatment groups
    - Setting of neutral expectations (e.g., script for programming)
- Outcome data collected, through use of an eDiary, prior to and independent of site interaction with the subject and prior to programming changes
- Rigorous screening process including saline (placebo) and lidocaine test injections prior to implantation

- Independent trial oversight
    - Data Monitoring Committee (DMC)
    - Independent Physician Adjudicator (IPA)
    - Independent statisticians
- Frequent monitoring and site audits
- Comprehensive training, including a requirement for up-to-date Good Clinical Practice (GCP) training for all site personnel
- Minimization of financial conflict of interest

2.1.1. Inclusion/Exclusion Criteria

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

1. Subject shall have a unilateral amputated lower limb for no less than 12 months. If the amputation needed revision within 12 months, patient could be enrolled if investigator documents that the amputation site has healed and subject's symptoms have stabilized.
2. Post-amputation pain shall be chronic (persistent over 6 months) and resistant to pain medications with a documented history within the subject's medical records.
3. Subject shall have frequent and recurring pain defined as no less than 4 episodes of pain ≥ 5 (based on numerical rating scale [NRS]) per week on average (to be confirmed with baseline pain diary).
4. Subject's typical pain episode should last no less than 60 minutes.
5. Subject shall demonstrate response to two injections, one regional nerve block and the other saline. Response to the regional nerve block is defined as greater than or equal to a 50% pain reduction by NRS at 20 minutes from administration of Lidocaine. An allowable, non-therapeutic response to saline is defined as less than 30% pain reduction by NRS 15 minutes after administration. NRS must be ≥ 5 before first injection.
6. Subject's regimen of drug therapy for pain shall be stable for no less than 4 weeks prior to implant and shall not change without approval of investigator until after their Month-3 visit. Subject shall sign a pain medication "contract" to confirm acceptance of guidelines for the use of pain medication.
7. Subject agrees not to replace or alter their prosthetic (if applicable) until after their Month-3 (primary endpoint) visit.
8. Subject is able to independently read and complete all questionnaires provided in English and use electronic diary during study.
9. Subject is willing and able to provide informed consent and comply with all procedures and assessments required by study protocol.
10. Subject, and caregiver if applicable, is able and willing to be available for study visits throughout the duration of the study, e.g., no planned relocation of residence or extended vacation during the study that would prevent compliance with study visit schedule.
11. Subject shall be 21 years of age or older (FDA definition of non-pediatric) and legally able to provide written informed consent.

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

1. Subject is currently implanted with any active implantable device including but not limited to: pacemaker, implantable cardiac defibrillator, implantable neurostimulator (e.g., peripheral or spinal cord stimulator), or implantable drug pump.
2. Subject has a source of pain other than post-amputation pain (incl. dysesthesia, cancer-related, visceral, angina, migraine, causalgia) which in the opinion of the investigator may interfere with the reporting of post-amputation pain.
3. Subject has medical contraindications to surgery, including but not limited to cardiovascular, pulmonary, renal, liver or hematological disorders, active inflammation, medical contraindication for general anesthesia (e.g., severe cardiopulmonary disease), compromised immune state (due to concomitant disease or medications such as chemotherapy or immunosuppressants), or anticoagulant medication that cannot be discontinued for perioperative period.
4. Uncontrolled diabetes as defined by HbA1c > 8.0.
5. Spasticity in their residual limb such that the subject cannot achieve volitional full range of motion (ROM) of joints on involved side.
6. Subject has skin graft or severe scarring over targeted implant site or any anatomical conditions that would prevent placement of the Altius System components.
7. Subject demonstrates an inability to discern differences in pain severity, report pain intensity and related information, or complete a pain diary.
8. Subject has a suspected or known allergy to any materials of the Altius System in tissue contact or Lidocaine (necessary for injection screen).
9. Subject has received therapeutic regional nerve block (e.g., anesthetic with steroid, and/or opioids) for post-amputation pain within 30 days prior to baseline visit.
10. Subject's usual seated posture includes sitting on the end of their stump.
11. Subject is a woman who is not using adequate contraception, is pregnant or breastfeeding, or intends to become pregnant during the course of the study.
12. Subject is currently participating or intends to participate in another investigational drug or device clinical study that may influence or interfere with the data that will be collected for this study.
13. Subject has a condition requiring MRI studies or diathermy after device implantation.
14. Subject has a history of any alcohol or substance abuse or dependence which has required prior medical treatment or intervention. Subject has active alcohol or substance abuse.
15. Subject has a condition that, in the opinion of the investigator, would interfere with study compliance (incl. unresolved issues of secondary gain) or subject's safety.
16. Subject has a life expectancy of less than 24 months.
17. Subject is diagnosed with or has untreated psychological conditions: borderline personality disorder, major depression disorder characterized by hospitalization within the prior year for a major depressive episode.
18. Subject has current diagnosis of any progressive neurological disease such as multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, rapidly progressive diabetic peripheral neuropathy, or any tumor of the nervous system.

19. Subjects with active local or systemic infection, prior recurrent bacterial infection, those who are immunocompromised or have high risk of infection due to other comorbidities.

2.1.2. Visit and Follow-Up Schedule

All subjects were consented during the baseline visit. Subjects were then assessed as to whether they fulfilled all eligibility criteria, including eDiary eligibility criteria and injection evaluation criteria. Subjects who failed one or more of the eligibility criteria at these pre-operative steps were considered screen failures. Subjects who withdrew consent or were withdrawn by the investigator prior to implant surgery were exited from the study and were not counted towards the 180-subject sample size.

At baseline, subjects had a physical exam, pregnancy test for women of child-bearing potential, medical history, baseline pain assessment and baseline quality of life (QoL) questionnaires. Subjects who passed the initial eligibility assessment were issued an eDiary device for recording pain intensity and medication and prosthetic use, if applicable. A baseline eDiary was collected for at least 14 calendar days with 2 or fewer days of missing data, including the severity, frequency, and duration of pain, medication consumption, and prosthetic use. Subjects whose eDiary confirmed frequent and recurring pain episodes of ≥ 5 (NRS) per week proceeded to the Injection Visit. At the injection visit, to assess the effect of placebo, 1 ml of saline was first injected as close to the nerve terminus as possible. An allowable, non-therapeutic, response to saline was defined as a reduction <30% on NRS at 15 minutes after administration. If the subject successfully passed the saline injection, 15 ml 2% lidocaine was then injected. A positive response to lidocaine was defined as a reduction ≥50% on NRS at 20 minutes after lidocaine administration, relative to the pain intensity prior to saline injection. Subjects who demonstrated a therapeutic response to saline or who did not respond to lidocaine were documented as screen failures.

Subjects who met all enrollment criteria, as judged by the investigator, including eDiary and injection criteria, proceeded to Altius System implant surgery. At 14 days post-surgery, after confirming contact between the programming system and the Altius IPG, subjects were randomized to one of the two treatment arms, and stimulation was programmed according to the subject's blinded treatment group assignment. Subjects then used the Altius System to treat pain episodes as needed (PRN), recording their pain level using NRS prior to Altius treatment and at 30-minutes and two-hours post-treatment. Subjects returned for follow-up visits, including QoL measures and pain medication use, at 21 days, 1 month, 42 days, 56 days, 3 months (primary endpoint), 105 days, 6 months, 9 months and 12 months (secondary endpoint). Subjects originally randomized to sham-control crossed over to active Altius treatment at Month 3. With their agreement, subjects are followed on an annual basis until End-of-Trial declaration.

The key timepoints for each assessment are shown in **Table 1** below. Adverse events were collected at every visit beginning at the baseline visit.

TABLE 1: QUEST SCHEDULE OF ASSESSMENTS

PARAMETER q	VISIT	Screening	Injection[1]	Implant	Day 14[2]	Day 21	Month 1	Day 42	Day 56	Month 3	Day 105[3]	Month 6	Month 9	Month 12	LTFU[4]	Revision[5]	Explant[6]
	POD Start	<0	<0	0	11	18	25	35	49	77	98	169	260	335	-30	NA	NA
	POD End				17	24	31	49	63	105	112	213	294	395	+30		
Informed consent		X															
Demographics		X															
Medical History		X															
Urine Dipstick[7]		X															
DASS		X															
BPI		X					X			X		X		X			
SF-12		X					X			X		X		X			
EQ-5D		X					X			X		X		X			
HbA1c[8]			X														
Sensorimotor Evaluation			X		X					X				X		X	X
Injection Evaluation			X														
Procedure Details				X													
Blinding Questionnaire					X		X			X		X					
PGIC										X		X		X			
NRS (eDiary)		X	X	X	X	X	X	X	X	X	X	X	X	X			
Pain Medications		X	X	X	X	X	X	X	X	X	X	X	X	X			
AE Assessment		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Programming					X	O	9	9	9	X	X	O	O	O	O	O	

DASS: Depression Anxiety Stress Scales; POD: Post-operative day; LTFU: Long-term follow-up; X: Required; O: As needed

[1] Injection evaluation scheduled after the subject passed two-week eDiary assessment.

[2] Randomization performed after device has been successfully activated. If Day 14 visit (randomization) was postponed due to inability to verify system integrity or delayed wound healing, subsequent visit windows would be adjusted accordingly.

[3] Day 105 visit for programming adjustment not required.

[4] During LTFU, subjects followed annually (every 365 days).

[5] Following revision, subject required to complete post-op follow-up visit 14 ±7 days after surgery

[6] Following explant, subject required to complete post-op follow-up visits 14 ±7 days and 183 ±30 days after surgery.

[7] Urine dipstick pregnancy test only required for subjects with child-bearing potential.

[8] HbA1c required for diabetic subjects prior to performing injection evaluation. A blood sample within 3 months of injection could be used.

[9] Programming adjustments during the Randomized testing phase were only made if necessary.

2.1.3. Critical Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint was the responder rate of subjects in each arm, active Altius treatment (Test) vs. sham-control treatment (Control), during the Randomized Testing phase of the study (Month 1 to Month 3). A responder was defined as a subject who demonstrates ≥50% reduction in NRS pain score from pre-treatment to 30-minutes post-treatment for ≥50% of all pain episodes in which the treatment was used. Study success was determined by a superiority test on the difference between responder rates in the Test and Control groups at Month 3.

Primary Safety Endpoint

The primary safety endpoint was the incidence of all Serious Adverse Events (SAEs), including Serious Adverse Device Events (SADEs), and Unanticipated (Serious) Adverse Device Events (UADE), from the time of injection through Month 3. The primary safety endpoint was determined at the conclusion of the Randomized Testing phase of the study, after all active participants completed the Month 3 Visit. The study was intended to show that the SAE rate for the active Altius treatment group is non-inferior to that of the sham-control group and that therapeutic electrical stimulation does not increase SAEs compared to non-therapeutic stimulation.

Secondary Effectiveness Endpoints

Intended for Labeling Claims

The study's secondary effectiveness endpoints intended to be tested for labeling claims were as follows (in hierarchical order for statistical testing):

- Change from baseline in Opioid Pain Medication Use (Morphine Equivalent Dose (MED)) at Month 3
- Change from baseline in Brief Pain Inventory (BPI) at Month 3
- Change from baseline in Short Form Health Survey (SF-12) Physical Component Summary (PCS) at Month 3
- Change from baseline in Short Form Health Survey (SF-12) Mental Component Summary (MCS) at Month 3
- Change from baseline in EuroQol (EQ-5D) at Month 3

Not Intended for Labeling Claims

The study's secondary effectiveness endpoints not intended to be tested for labeling claims were as follows:

- Primary effectiveness beyond Month 3 through Month 12
- Pain Relief after 2 Hours
- Pain Days per Week
- Change from baseline in Non-Opioid Analgesic Pain Medication Use through Month 12
- Change from baseline in Opioid Pain Medication Use (Morphine Equivalent Dose (MED)) through Month 12

- Change from baseline in Brief Pain Inventory (BPI) through Month 12
- Change from baseline in EuroQol (EQ-5D) through Month 12
- Change from baseline in Short Form Health Survey (SF-12) Physical Component Summary (PCS) through Month 12
- Change from baseline in Short Form Health Survey (SF-12) Mental Component Summary (PCS) through Month 12
- Change from baseline in Patient Global Impression of Change (PGIC)
- Session Success Rate
- Composite Responder Rate (Reduction in pain AND absence of increase in medication usage)

Secondary Safety Endpoints

The secondary safety endpoint was the incidence of all adverse events including non-serious adverse events, non-serious adverse device effects, SAEs, SADEs, and UADE, from time of injection through the Month 12 visit.

2.2. Accountability of PMA Cohort

At the time of the database lock for this PMA report, 183 subjects underwent surgery to implant the Altius System (Safety population). Three subjects were anesthetized for index surgery, but the Altius device was not implanted, in two cases because the target nerve could not be located and in one case because there was insufficient sciatic nerve to support implant of the cuff electrode. Therefore, 180 subjects were implanted with the Altius System. Two subjects were implanted with the Altius device but were not randomized; one died from pulmonary embolism on POD 5, and the other had the device explanted prior to activation because of axonal discontinuity at the target nerve. Thus, 178 subjects were randomized, 87 to active Altius treatment (Test) and 91 to sham-control (Control) (ITT population). Eight of those 178 subjects (two Test and six Control) never used the Altius device, so 170 subjects (85 Test and 85 Control) completed the randomized testing phase and were evaluable for the primary effectiveness endpoint at Month 3 (FAS population). The Month 12 visit was completed by 146 of 149 eligible subjects. Refer to

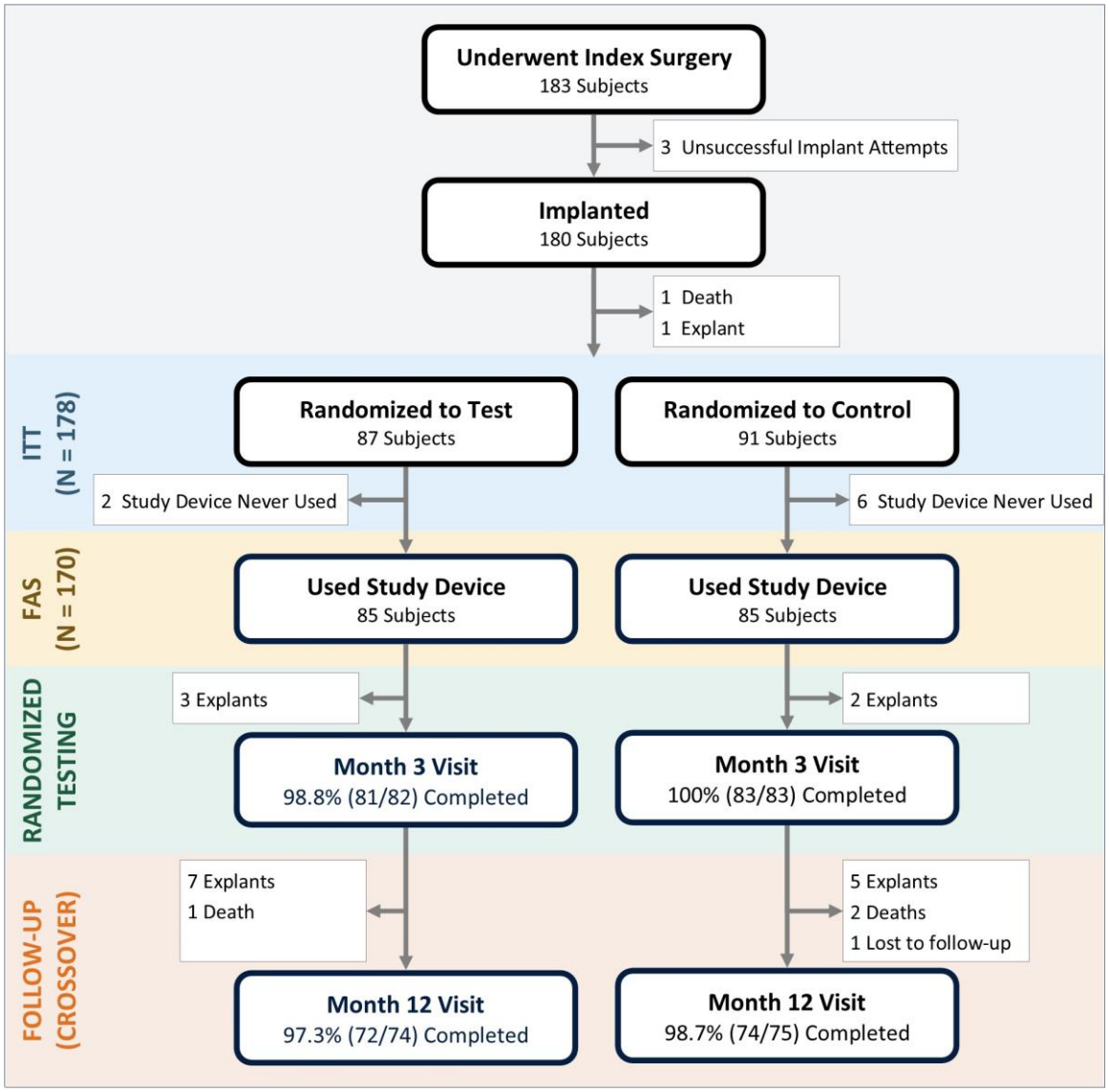

FIGURE 1: SUBJECT DISPOSITION BY VISIT THROUGH MONTH 12

2.3. Study Population Demographics and Baseline Parameters

Table 2 summarizes the key demographic, medical history and baseline parameters for the FAS population. The two treatment arms were well balanced across all baseline factors.

ALTIUS SYSTEM CLINICAL SUMMARY

TABLE 2: KEY DEMOGRAPHICS, MEDICAL HISTORY AND BASELINE PARAMETERS (FAS)

	Test **N = 85** Mean ± SD (Min, Max) or n (%)	**Control** **N = 85** Mean ± SD (Min, Max) or n (%)	**Total FAS** **N = 170** Mean ± SD (Min, Max) or n (%)	**p-value [1]**
Age (years)	58.1 ± 12.21 (26, 84)	57.9 ± 12.57 (22, 87)	58.0 ± 12.35 (22, 87)	0.916
Sex				
Male	60.0% (51/85)	60.0% (51/85)	60.0% (102/170)	>0.999
Female	40.0% (34/85)	40.0% (34/85)	40.0% (68/170)	
Race				
American Indian or Alaska Native	2.4% (2/85)	1.2% (1/85)	1.8% (3/170)	0.899
Asian	0.0% (0/85)	0.0% (0/85)	0.0% (0/170)	
Black or African American	14.1% (12/85)	11.8% (10/85)	12.9% (22/170)	
Native Hawaiian or Other Pacific Islander	1.2% (1/85)	0.0% (0/85)	0.6% (1/170)	
White	77.6% (66/85)	83.5% (71/85)	80.6% (137/170)	
Other	0.0% (0/85)	0.0% (0/85)	0.0% (0/170)	
Multiple	2.4% (2/85)	1.2% (1/85)	1.8% (3/170)	
Unknown	2.4% (2/85)	2.4% (2/85)	2.4% (4/170)	
Ethnicity – Hispanic or Latino	1.2% (1/85)	0.0% (0/85)	0.6% (1/170)	>0.999
BMI (kg/m²)	30.5 ± 7.75 (16, 50)	28.8 ± 5.73 (15, 45)	29.7 ± 6.85 (15, 50)	0.098
Level of Amputation				
Above knee (AKA)	44.7% (38/85)	41.2% (35/85)	42.9% (73/170)	0.757
Below knee (BKA)	55.3% (47/85)	58.8% (50/85)	57.1% (97/170)	
Cause of Amputation				
Dysvascular	42.4% (36/85)	41.2% (35/85)	41.8% (71/170)	0.839
Trauma	43.5% (37/85)	41.2% (35/85)	42.4% (72/170)	
Other	14.1% (12/85)	17.6% (15/85)	15.9% (27/170)	
Time From Amputation to Baseline Visit (Months)	93.2 ± 107.46 (12.0, 615.0)	72.6 ± 71.17 (12.0, 373.0)	82.9 ± 91.45 (12.0, 615.0)	0.142
Worst daily limb pain (0-10)	9.1 ± 0.98 (85) (6.0, 10.0)	9.1 ± 1.05 (85) (6.0, 10.0)	9.1 ± 1.01 (170) (6.0, 10.0)	>0.999
Worst daily limb pain (categories)				
No Pain (0)	0.0% (0/85)	0.0% (0/85)	0.0% (0/170)	0.663
Mild (1-3)	0.0% (0/85)	0.0% (0/85)	0.0% (0/170)	
Moderate (4-6)	2.4% (2/85)	2.4% (2/85)	2.4% (4/170)	
Severe (7-9)	57.6% (49/85)	50.6% (43/85)	54.1% (92/170)	
Worst Possible Pain (10)	40.0% (34/85)	47.1% (40/85)	43.5% (74/170)	
Average daily limb pain (0-10)	6.1 ± 1.45 (2.7, 10.0)	5.9 ± 1.47 (3.1, 10.0)	6.0 ± 1.46 (2.7, 10.0)	0.224

ALTIUS SYSTEM CLINICAL SUMMARY

	Test **N = 85** Mean ± SD (Min, Max) or n (%)	**Control** **N = 85** Mean ± SD (Min, Max) or n (%)	**Total FAS** **N = 170** Mean ± SD (Min, Max) or n (%)	**p-value [1]**
Average daily limb pain (categories)				
No Pain (0)	0.0% (0/85)	0.0% (0/85)	0.0% (0/170)	0.419
Mild (1-3)	3.5% (3/85)	7.1% (6/85)	5.3% (9/170)	
Moderate (4-6)	62.4% (53/85)	64.7% (55/85)	63.5% (108/170)	
Severe (7-9)	32.9% (28/85)	24.7% (21/85)	28.8% (49/170)	
Worst Possible Pain (10)	1.2% (1/85)	3.5% (3/85)	2.4% (4/170)	
Pain duration type				
Episodic or Breakthrough Pain	36.9% (31/84)	35.3% (30/85)	36.1% (61/169)	0.873
Persistent; It Builds and Remains for Most of the Day	63.1% (53/84)	64.7% (55/85)	63.9% (108/169)	
Limb pain type				
Stump Only	6.0% (5/84)	3.6% (3/84)	4.8% (8/168)	0.833
Phantom Only	9.5% (8/84)	7.1% (6/84)	8.3% (14/168)	
Stump is Much Worse	10.7% (9/84)	15.5% (13/84)	13.1% (22/168)	
Phantom is Much Worse	27.4% (23/84)	27.4% (23/84)	27.4% (46/168)	
Both Stump and Phantom Pain are Bad	46.4% (39/84)	46.4% (39/84)	46.4% (78/168)	
Hours Per Day of Prosthetic Leg Use				
0	11.9% (10/84)	15.3% (13/85)	13.6% (23/169)	0.152
>0 to 4	13.1% (11/84)	14.1% (12/85)	13.6% (23/169)	
>4 to 8	27.4% (23/84)	11.8% (10/85)	19.5% (33/169)	
>8 to 12	19.0% (16/84)	20.0% (17/85)	19.5% (33/169)	
>12 to 16	16.7% (14/84)	28.2% (24/85)	22.5% (38/169)	
>16 to 20	4.8% (4/84)	5.9% (5/85)	5.3% (9/169)	
>20 to < 24	0.0% (0/84)	0.0% (0/85)	0.0% (0/169)	
All Day	0.0% (0/84)	1.2% (1/85)	0.6% (1/169)	
N/A - no prosthetic leg	7.1% (6/84)	3.5% (3/85)	5.3% (9/169)	
Alcohol Abuse				
Current condition	0.0% (0/85)	0.0% (0/84)	0.0% (0/169)	0.117
Past, resolved	1.2% (1/85)	6.0% (5/84)	3.6% (6/169)	
No prior history	98.8% (84/85)	94.0% (79/84)	96.4% (163/169)	
Anxiety				
Current condition	41.2% (35/85)	50.6% (43/85)	45.9% (78/170)	0.409
Past, resolved	1.2% (1/85)	2.4% (2/85)	1.8% (3/170)	
No prior history	57.6% (49/85)	47.1% (40/85)	52.4% (89/170)	
Depression				
Current condition	44.7% (38/85)	53.6% (45/84)	49.1% (83/169)	0.311
Past, resolved	4.7% (4/85)	7.1% (6/84)	5.9% (10/169)	
No prior history	50.6% (43/85)	39.3% (33/84)	45.0% (76/169)	

ALTIUS SYSTEM CLINICAL SUMMARY

	Test **N = 85** Mean ± SD (Min, Max) or n (%)	**Control** **N = 85** Mean ± SD (Min, Max) or n (%)	**Total FAS** **N = 170** Mean ± SD (Min, Max) or n (%)	**p-value [1]**
Diabetes				
Current condition	40.0% (34/85)	28.6% (24/84)	34.3% (58/169)	0.237
Past, resolved	1.2% (1/85)	1.2% (1/84)	1.2% (2/169)	
No prior history	58.8% (50/85)	70.2% (59/84)	64.5% (109/169)	
Peripheral Neuropathy				
Current condition	29.4% (25/85)	27.4% (23/84)	28.4% (48/169)	0.799
Past, resolved	1.2% (1/85)	0.0% (0/84)	0.6% (1/169)	
No prior history	69.4% (59/85)	72.6% (61/84)	71.0% (120/169)	
Peripheral Vascular Disease				
Current condition	27.1% (23/85)	29.8% (25/84)	28.4% (48/169)	0.915
Past, resolved	3.5% (3/85)	3.6% (3/84)	3.6% (6/169)	
No prior history	69.4% (59/85)	66.7% (56/84)	68.0% (115/169)	
Taking Any Rescue Medication at Baseline	36.5% (31/85)	37.6% (32/85)	37.1% (63/170)	
Taking Rescue Opioid and Opioid/Nonopioid Combination at Baseline	32.9% (28/85)	20.0% (17/85)	26.5% (45/170)	
Taking Rescue Anticonvulsant at Baseline	2.4% (2/85)	7.1% (6/85)	4.7% (8/170)	
Taking Any Routine Medication at Baseline	63.5% (54/85)	49.4% (42/85)	56.5% (96/170)	
Taking Routine Opioid and Opioid/Nonopioid Combination at Baseline	28.2% (24/85)	20.0% (17/85)	24.1% (41/170)	
Taking Routine Anticonvulsant at Baseline	50.6% (43/85)	47.1% (40/85)	48.8% (83/170)	
[1] Statistical comparison between treatment groups for categorical variables performed using two-sided Fisher's exact test and for continuous variables two-sided two sample t-test. Significance for both evaluated at the 0.05 level.				

2.4. Safety & Effectiveness Results

2.4.1. Safety Results

Primary Safety Endpoint – All SAEs through Month 3

The primary safety endpoint was the incidence of all serious adverse events (SAEs), including serious adverse device-related events (SADEs) and unanticipated adverse device effects (UADEs), from the time of injection through the conclusion of the blinded Randomized Testing phase at Month 3. The primary safety analysis was based on the Safety population of subject who underwent surgery (N=183) and was repeated in the ITT population of subjects who were implanted and randomized (N=178).

Among the 183 Safety subjects (**Table 3**), 8 SAEs that were device-related (SADE) occurred in 8 subjects (4.4%), and 20 procedure-related SAEs occurred in 15 subjects (8.2%). The overall SAE rate was 26.2% (48/183) in the Safety population.

In the ITT population (**Table 4**), N=178 subjects (87 Test, 91 Control), 3 device-related SAEs occurred in 3 Test subjects (3.4%) and 5 occurred in 5 Control subjects (5.5%). Procedure-related SAEs occurred in 8 Test subjects (9.2%) and 7 Control subjects (7.7%). The overall SAE rate was 28.7% in the Test arm and 24.2% in the Control arm in the ITT population. There was no difference between the two treatment arms with respect to device-related, procedure-related and overall SAEs, based on 95% confidence intervals (CI). These results indicate that a therapeutic level of nerve stimulation (Test) did not cause more SAEs than a sub-therapeutic dose (Control). There were no UADEs.

As summarized in **Table 4,** the most common device-related SAEs were infections and wound-related complications related to the IPG and/or cuff electrode implant sites. After an initial spike in infection/wound-related events during the early part of the QUEST study and the implementation of infection control measures, the rate of such events declined to ≤5% among the last 159 implanted subjects.

TABLE 3: PRIMARY SAFETY ENDPOINT - ALL SAES FROM INJECTION TO MONTH 3, SAFETY POPULATION

	Implanted		Not Implanted		Safety Population	
	Number of Events	**Number of Subjects with Event N = 180**	**Number of Events**	**Number of Subjects with Event N = 3**	**Number of Events**	**Number of Subjects with Event N = 183**
All Serious Adverse Events	65	26.7% (48/180)	0	0.0% (0/3)	65	26.2% (48/183)
Serious Device Related AEs [5][6]	8	4.4% (8/180)	0	0.0% (0/3)	8	4.4% (8/183)
Serious Procedure Related AEs [5]	20	8.3% (15/180)	0	0.0% (0/3)	20	8.2% (15/183)
UADEs	0	0.0% (0/180)	0	0.0% (0/3)	0	0.0% (0/183)

TABLE 4: PRIMARY SAFETY ENDPOINT - ALL SAES AND DEVICE-RELATED SAES BY TYPE, FROM INJECTION TO MONTH 3, ITT POPULATION

	Test			Control			
	Number of Events	**Number of Subjects with Event N = 87**	**95% CI [3]**	**Number of Events**	**Number of Subjects with Event N = 91**	**95% CI [3]**	**Difference Test - Control (95% CI)**
All Serious Adverse Events	33	28.7% (25/87)	19.54, 39.43	31	24.2% (22/91)	15.81, 34.28	4.56% (-8.32%, 17.34%)
Serious Device Related AEs	3	3.4% (3/87)	0.72, 9.75	5	5.5% (5/91)	1.81, 12.36	-2.05% (-9.15%, 4.90%)
Serious Procedure Related AEs	11	9.2% (8/87)	4.05, 17.32	9	7.7% (7/91)	3.15, 15.21	1.50% (-7.09%, 10.33%)
UADEs	0	0.0% (0/87)	N/A	0	0.0% (0/91)	N/A	N/A
Serious Device Related AEs by Event Type (MedDRA coded)							
Gastrointestinal disorders	0	0.0% (0/87)		1	1.1% (1/91)		
Abdominal pain	0	0.0% (0/87)		1	1.1% (1/91)		
General disorders and administration site conditions	2	2.3% (2/87)		1	1.1% (1/91)		
Discomfort	1	1.1% (1/87)		0	0.0% (0/91)		

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	Test			Control			
	Number of Events	**Number of Subjects with Event N = 87**	**95% CI [3]**	**Number of Events**	**Number of Subjects with Event N = 91**	**95% CI [3]**	**Difference Test - Control (95% CI)**
Medical device discomfort	1	1.1% (1/87)		0	0.0% (0/91)		
Medical device site pain	0	0.0% (0/87)		1	1.1% (1/91)		
Infections and infestations	0	0.0% (0/87)		2	2.2% (2/91)		
Postoperative wound infection	0	0.0% (0/87)		2	2.2% (2/91)		
Injury, poisoning and procedural complications	0	0.0% (0/87)		1	1.1% (1/91)		
Wound dehiscence	0	0.0% (0/87)		1	1.1% (1/91)		
Product issues	1	1.1% (1/87)		0	0.0% (0/91)		
Device extrusion	1	1.1% (1/87)		0	0.0% (0/91)		

Secondary Safety Endpoint – All SAEs from Month 3 to Month 12

The incidence of all SAEs, including SADEs and UADEs, from Month 3 to Month 12 was analyzed in the ITT population (**Table 5**). The Month-3-to-12 SADE rate was 3.4% in the Test arm and 5.5% in the Control arm. There was no difference between the two treatment arms with respect to SADEs from Month 3 to Month 12, based on 95% CI.

TABLE 5: ADDITIONAL SAFETY PARAMETERS – ALL SAES FROM MONTH 3 TO MONTH 12, ITT POPULATION

	Test			Control			
	Number of Events	**Number of Subjects with Event N = 87**	**95% CI [3]**	**Number of Events**	**Number of Subjects with Event N = 91**	**95% CI [3]**	**Difference (95% CI) [4]**
All Serious Adverse Events	29	24.1% (21/87)	15.60, 34.50	35	24.2% (22/91)	15.81, 34.28	-0.04% (-12.49%, 12.51%)
Serious Device Related AEs [5][6]	3	3.4% (3/87)	0.72, 9.75	5	5.5% (5/91)	1.81, 12.36	-2.05% (-9.15%, 4.90%)
Serious Procedure Related AEs [5]	2	2.3% (2/87)	0.28, 8.06	1	1.1% (1/91)	0.03, 5.97	1.20% (-3.94%, 6.97%)
Serious Explant or Revision of Study Device Related AEs [5]	0	0.0% (0/87)	0.00, 4.15	0	0.0% (0/91)	0.00, 3.97	N/A

Deaths

As of the data cut-off date, 04-Jan-2023, 13 subjects were reported to have died during the QUEST study. Nine of the 13 died more than a year after Altius System implantation. Ten deaths (3 respiratory failure/arrest, 2 cancer, 2 cardiac disorder/failure, 1 hepatic cirrhosis,1 suicide, 1 COVID-19 infection) were determined to be not related to the Altius device or the implantation surgery, and 3 deaths (1 pulmonary embolism, 1 cerebrovascular accident, 1 unknown cause) were adjudicated as unknown. There were no deaths attributed to the Altius System or the associated surgery.

Revisions & Explants

In the FAS population, 17 subjects (10 Test, 7 Control) had the Altius IPG and/or cuff electrode(s) explanted within 12 months of index surgery. Four explants were the result of subject request (1 related to insufficient pain relief in control subject; 1 due to need for MRI; 2 no reason specified); 5 due to implant site infection or wound dehiscence; 6 due to device-related complication (e.g., discomfort, device extrusion, wound dehiscence); 1 due to IS-1 connector failure; and 1 due to unrelated surgery.

In the same population and timeframe, 21 subjects (11 Test, 10 Control) had one or more revisions of the Altius IPG and/or cuff electrode(s). The primary reason for revision was IS-1 connector failure (N=10 subjects); medical device site pain or discomfort (5); infection at the implant site (4); cuff sizing correction (1); and cosmetic reason (1).

For both explants and revisions, the need for intervention was independent of treatment group assignment. Corrective actions were taken during the study to address infection/wound complication events and the IS-1

connector issue. While the revision/explant rate seen in the QUEST study is acceptable and consistent with similar AIMDs, this rate is expected to be lower in commercial use as a result of the mitigations.

Safety Conclusions

The overall rate of safety events associated with the Altius System summarized below.

- **The occurrence of overall SAEs, SADEs and procedure-related SAEs was similar between the Test and Control groups, indicating no adverse effect from active HFAC stimulation.**
- There were no UADEs and no deaths attributable to the Altius System.
- The rate of SADEs was low at 4.4%.
- All SADEs were resolved during the study.

The rate of overall SAEs is attributed to the medical complexity of this post-amputation population, which is prone to co-morbidities and poor overall health.

2.4.2. Effectiveness Results

Analysis Populations

The primary effectiveness analysis and all secondary analyses, whether intended for labeling or not, were performed on the FAS population (N=170; 85 Test, 85 Control) and key endpoints were confirmed in the Per-Protocol (PP) population (N=156; 76 Test, 80 Control). Because Control subjects crossed over to Test (active Altius therapy) at Month 3, some Month 3-12 analyses were also performed in the combined Test + Control FAS cohort.

Primary Effectiveness Analysis

The study's primary effectiveness endpoint was the responder rate of subjects in each arm, Test vs. Control, during the Randomized Testing phase of the study (Month 1 through Month 3). Study success was determined by a superiority test on the difference between responder rates in the Control and Test groups at Month 3, using logistic regression. The logistic regression model controlled for amputation etiology, amputation location, pain type, baseline pain intensity and baseline pain duration.

The QUEST study met its pre-specified primary endpoint, demonstrating superior pain relief with the active Altius treatment compared to control, and the study is deemed a success with respect to effectiveness.

In the Test arm, 24.7% (21/85) of subjects were responders, compared to 7.1% (6/85) of Control subjects (**Table 6**). The absolute difference between the treatment arms was 17.6% (95% CI: 7.0%, 28.3%) and was highly statistically significant using a one-sided significance level (alpha) of 0.025 (p=0.002). Subjects undergoing active Altius treatment were >3 times more likely to experience significant pain relief than subjects who were randomized to the sham-control arm.

TABLE 6: PRIMARY EFFECTIVENESS ANALYSIS – RESPONDER RATE AT 30 MINUTES – THROUGH 3 MONTHS, FAS POPULATION

	Test Group N = 85	Control Group N = 85	Difference Test - Ctrl (95% CI)	One-sided p-value [1]
Primary Performance Endpoint - Responders [2] [3] [4]	24.7% (21/85)	7.1% (6/85)	17.6% (7.0%, 28.3%)	0.002
95% CI	(15.5%, 33.9%)	(1.6%, 12.5%)		

[1] The responder rate was compared between treatment groups using logistic regression controlling for the following covariates: Etiology (dysvascular, trauma, other), Amputation Location (AKA, BKA), Pain Type (phantom, stump, both), Baseline Pain Intensity (5-6, 7-10) defined as the average of the end-of-day worst pain scores from the subject's e-diary compliant eligibility window, and Baseline Pain Duration (episodic, persistent). Significance is evaluated using a one-sided test with alpha level 0.025.
[2] A responder was defined as any subject who attained ≥50% pain reduction at the 30-minute follow-up assessment in ≥50% of the treatment sessions during the Randomized Testing phase of the study.
[3] Missing pain score at 30 minutes for a particular completed treatment session was considered a failure for that session. Treatment sessions that were interrupted with rescue (p.r.n.) pain medications utilize the assessment of pain at the time of rescue medication, missing observations were considered a failure for that session.
[4] Subjects who were randomized to receive treatment but who terminated prior to their scheduled Month 3 Visit (Day 91 + 14 days post-implantation) were determined to be a responder or non-responder based on their available data prior to termination.

The primary effectiveness results were demonstrated to be robust, with the same outcome in favor of active Altius treatment found in three sensitivity analyses, a multiple imputation analysis and a tipping point (ITT Population) analysis. The primary results were also confirmed in the PP population.

The Cumulative Distribution Function (CDF) is a method of evaluating patient responses over a full range of response levels, utilizing the same data as the primary endpoint. Rather than relying on one cut-point for evaluation, the CDF provides a more accurate reflection of the full nature of the data. This analysis, presented in **Figure 2,** shows a consistent advantage of Test over Control in treatment effect at all proportions of sessions from just above 0% to almost 100%. The Altius treatment effect is robust, with a similar treatment effect across a wide range of session effect. In addition, the significant treatment effect is preserved through that effective range.

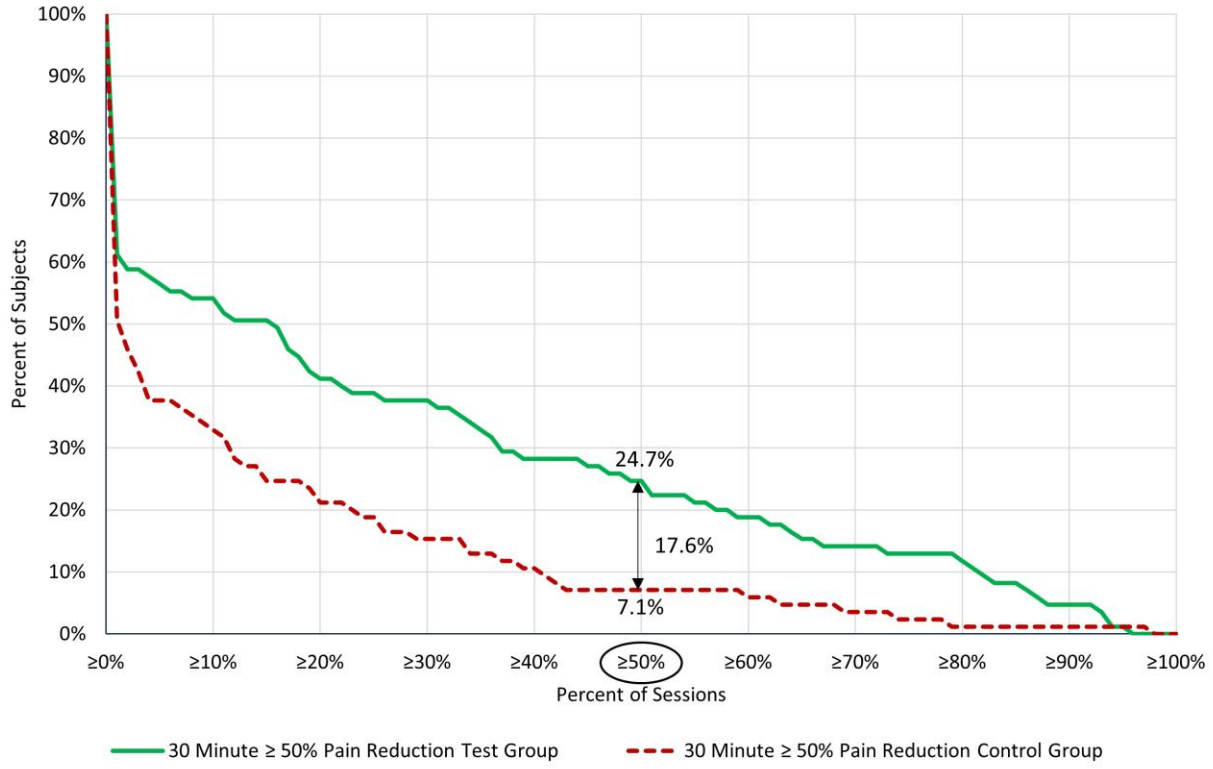

FIGURE 2: CUMULATIVE RESPONDER DISTRIBUTION AT 30 MINUTES AS A FUNCTION OF % SESSIONS, FAS POPULATION

Secondary Analyses of the Primary Effectiveness Endpoint

To evaluate durability of Altius treatment effect past 30 minutes, the responder rate, using the same criteria of ≥50% pain reduction in ≥50% sessions, was calculated for pain scores recorded at two hours post-treatment (**Table 7**)**.** The treatment effect of Test vs. Control was 25.8% (95% CI: 11.5%, 40.2%), with 48.1% of Test subjects responding to treatment vs. 22.2% of Contol subjects; this difference was highly statistically significant ($p<0.001$), confirming that Altius treatment is durable for at least two hours after device use.

TABLE 7: RESPONDER RATE AT TWO HOURS – THROUGH 3 MONTHS, FAS POPULATION

	Test Group N = 85	Control Group N = 85	Difference Test - Ctrl (95% CI)	One-sided p-value [1]
Primary Performance Endpoint at 120 Minutes - Responders [2] [3] [4]	48.1% (37/77)	22.2% (18/81)	25.8% (11.5%, 40.2%)	<0.001
95% CI	(36.9%, 59.2%)	(13.2%, 31.3%)		

[1] The responder rate was compared between treatment groups using logistic regression controlling for the following covariates: Etiology (dysvascular, trauma, other), Amputation Location (AKA, BKA), Pain Type (phantom, stump, both), Baseline Pain Intensity (5-6, 7-10) defined as the average of the end-of-day worst pain scores from the subject's e-diary compliant eligibility window, and Baseline Pain Duration (episodic, persistent). Significance is evaluated using a one-sided test with alpha level 0.025.
[2] A responder was defined as any subject who attained ≥50% pain reduction at the 120-minute follow-up assessment in ≥50% of the treatment sessions during the Randomized Testing phase of the study.
[3] Missing pain score at 120 minutes for a particular completed treatment session was excluded from the analysis. Treatment sessions that were interrupted with rescue (p.r.n.) pain medications utilize the assessment of pain at the time of rescue medication, missing observations were considered a failure for that session.
[4] Subjects who were randomized to receive treatment but who terminated prior to their scheduled Month 3 Visit (Day 91 + 14 days post-implantation) were determined to be a responder or non-responder based on their available data prior to termination.

Secondary Effectiveness Analyses Intended for Labeling

Five secondary effectiveness endpoints were designated as being intended for labeling claims. All were analyzed based on the FAS population, and no imputation for missing data was used; analyses were conducted based on available data. The secondary endpoints intended for labeling were prioritized and tested in a hierarchical gatekeeping manner, at a one-sided 0.025 significance level, to control the maximum overall Type I error rate. The secondary effectiveness endpoints for labeling are summarized in **Table 8** with the outcome of the remaining three secondary effectiveness endpoints in the last three rows. **Active Altius subjects (Test) demonstrated significant reduction in opioid use and significant improvement in pain interference to ADL compared to sham-control.** Details of the first two successful endpoints are provided below.

TABLE 8: SUMMARY OF SECONDARY EFFECTIVENESS ENDPOINTS FOR LABELING

Endpoint	Outcome T_t vs. C_t (P-Value)	Statistical Success
Change from baseline in opioid pain medication at Month 3, FAS	-5.3 ± 13.76 vs. -1.3 ± 6.80 (**0.012**)	**Yes** Criteria for labeling claim met
Change from baseline in pain interference to ADL at Month 3, FAS	-2.3 ± 2.60 vs. -1.3 ± 2.40 (**0.010**)	**Yes** Criteria for labeling claim met
Change from baseline in SF-12 PCS at Month 3, FAS	4.1 ± 9.05 vs. 4.3 ± 7.19 (0.571)	No
Change from baseline in SF-12 MCS at Month 3, FAS	2.3 ± 8.71 vs. -2.1 ± 12.11 (**0.004**)	**Yes** Criteria for labeling claim not met
Change from baseline in EuroQoL-5D at Month 3, FAS	0.043 ± 0.163 vs. 0.035 ± 0.183 (0.395)	No

Change from Baseline in Opioid Pain Medication Use at Month 3

Opioid pain medication use was assessed using morphine equivalent dose (MED) for both rescue and routine opioid pain medications. The average daily MED (MED/day) was calculated for each subject across two weeks at baseline and the two weeks preceding Month 3. Two subjects, one in each treatment arm, had extreme decreases in opioid pain medication use, with a change from baseline in average daily MED ≥6 standard deviations from the mean, and extenuating circumstances regarding opiate use and were excluded from the analysis. Test subjects had a mean change from baseline of -5.3±13.76 MED compared to -1.3±6.80 in the Control arm (**Table 9:)** a statistically significant difference (p=0.012). Among subjects who reported opioid use at baseline and any utilization (even if zero) at Month 3, there was a 55.1% decrease from baseline to Month 3 in the Test arm and a 42.2% decrease in the Control arm. See also **Figure 3.**

TABLE 9: SECONDARY EFFECTIVENESS ENDPOINT FOR LABELING CLAIM – CHANGE FROM BASELINE IN OPIOID PAIN MEDICATION USE AT MONTH 3 – EXCLUDING OUTLIERS, FAS POPULATION [1]

	2 Weeks at Baseline		2 Weeks Before Month 3		
	Test N=84	**Control N=84**	**Test N=76**	**Control N=78**	**p-value [3]**
Average Daily MED [2]					
Mean ± SD (N)	19.6 ± 38.25 (84)	8.9 ± 23.98 (84)	13.9 ± 36.33 (76)	8.2 ± 24.14 (78)	
Median (Min, Max)	0.0 (0.0, 228.6)	0.0 (0.0, 165.4)	0.0 (0.0, 245.7)	0.0 (0.0, 163.0)	
Mean Change from Baseline ± SD					
Mean ± SD (N)			-5.3 ± 13.76 (76)	-1.3 ± 6.80 (78)	0.012

	2 Weeks at Baseline		2 Weeks Before Month 3		
	Test N=84	**Control N=84**	**Test N=76**	**Control N=78**	**p-value [3]**
Median (Min, Max)			0.0 (-60.0, 22.5)	0.0 (-18.8, 37.1)	
Mean % Change from Baseline ± SD					
Mean ± SD (N)			-55.1 ± 46.18 (34)	-42.2 ± 41.79 (23)	
Median (Min, Max)			-68.0 (-100.0, 36.4)	-33.3 (-100.0, 24.7)	

[1] Includes FAS population excluding subjects with a decrease of 6 or more standard deviations from the mean without a minimum requirement for days reported within the Month 3 Visit Window. One (1) Test Group subject (05-021) and one (1) Control Group subject (27-031) were categorized as outliers. There were 6 subjects who did not have a Month 3 Visit and as a result could not be counted at the Month 3 timepoint. An additional 8 subjects had a Month 3 Visit but did not report their medication use at any time during the 2 week window and were not included in the Month 3 timepoint.
[2] Average daily morphine equivalent dose (MED), both rescue (p.r.n.) and routine opioid pain medications, calculated for each subject across two weeks at Baseline and preceding Month 3.
[3] One-sided p-value reported for the comparison between Test and Control groups on the mean change from baseline in per-subject average MED/day using an ANOVA model.
Significance evaluated at the 0.025 level, if and only if the primary effectiveness endpoint is achieved.

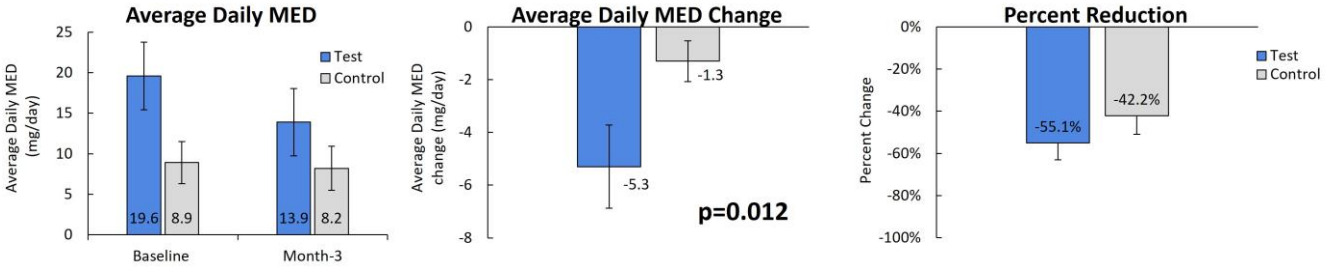

FIGURE 3: AVERAGE DAILY MED AT BASELINE AND MONTH 3 (LEFT), CHANGE FROM BASELINE IN IN DAILY MED AT MONTH 3 (MIDDLE) AND % REDUCTION FROM BASELINE TO MONTH 3 (RIGHT) BY TREATMENT ARM – EXCLUDING OUTLIERS, FAS POPULATION

Change from Baseline in Pain Interference to ADL at Month 3

Pain interference to activities of daily living (ADL), a measure of pain-related QoL, was calculated using the mean of the seven items from the BPI Interference scale, which include General Activity, Mood, Walking Ability, Normal Work, Relationships with Other People, Sleep, and Enjoyment of Life. Each item was scored on a scale of 0 - 10, by intervals of one, where 0 indicates 'Does not interfere' and 10 indicates 'Completely Interferes'. The mean change in pain interference to ADL from baseline to Month 3, including all FAS subjects (**Table 10**), was -2.3±2.60 in the Test arm and -1.3±2.40 in the Control arm, indicating a reduction in pain interference to ADL in both study arms, a statistically significant difference in favor of Test (p=0.010), and a clinically meaningful improvement in pain (38% improvement in pain interference to ADL for Test subjects vs. 22% for Control subjects).

TABLE 10: SECONDARY EFFECTIVENESS ENDPOINT FOR LABELING CLAIM – CHANGE FROM BASELINE IN PAIN INTERFERENCE TO ADL AT MONTH 3, FAS POPULATION

	Baseline		Month 3		
	Test N=85	**Control N=85**	**Test N=81**	**Control N=83**	**p-value [3]**
BPI-Interference Summary Score [1] [2]					
Mean ± SD (N)	6.1 ± 2.11 (85)	5.8 ± 1.94 (85)	3.7 ± 2.70 (81)	4.4 ± 2.50 (83)	
Median (Min, Max)	6.1 (1.4, 10.0)	6.0 (2.0, 10.0)	3.6 (0.0, 9.9)	4.4 (0.0, 9.4)	
Quartiles (1,3)	(4.9 ,7.7)	(4.4 ,7.1)	(1.4 ,5.7)	(2.0 ,6.1)	
Mean Change from Baseline ± SD					0.010
Mean ± SD (N)			-2.3 ± 2.60 (81)	-1.3 ± 2.40 (83)	
Median (Min, Max)			-1.9 (-9.0, 3.1)	-1.0 (-6.7, 4.1)	

[1] Calculated as the mean of 7 Brief Pain Inventory items: General Activity, Mood, Walking Ability, Normal Work, Relations with Other People, Sleep, Enjoyment of Life. Each item was scored on a scale of 0 - 10, by intervals of one, where 0 indicates 'Does not interfere' and 10 indicates 'Completely Interferes'.
[2] Subjects missing >0% but <50% of the responses to these 7 items at a given visit had missing responses imputed with the median of the remaining responses at that visit prior to calculating the 7-item average. Subjects missing more than 50% of the responses at a given visit were considered to have missing BPI-interference score at that visit.
[3] One-sided p-value reported for the comparison between Test and Control groups on the mean change from baseline in per-subject BPI-Interference Summary Score using ANOVA. Significance evaluated at the 0.025 level, if and only if the 1) primary effectiveness endpoint and 2) change from baseline in opioid pain medication at Month 3 are achieved.

Secondary Effectiveness Analyses Not Intended for Labeling

A number of additional secondary effectiveness analyses were performed but were not intended for labeling claims, as summarized below:

- The responder rate in crossed-over Control subjects at Month 6, 22.1%, was similar to the Month 3 Test responder rate, 24.7%, and indicates that control subjects had a numerically and clinically meaningful improvement in pain after Altius stimulation was increased to therapeutic levels at cross-over.
- Test subjects experienced significant additional pain relief from 30 minutes to two hours post-stimulation at all follow-up timepoints, Months 3, 6 and 12, reflecting durability of the Altius treatment effect, as did Control subjects at Months 6 and 12.
- Subjects in both treatment arms began the study reporting pain almost 7 days per week. By Month 12, both treatment arms demonstrated a reduction of approximately 3.5 pain days per week, a 50%+ reduction in pain days compared to baseline.
- There was a consistent, statistically significant and clinically meaningful decline in daily opioid pain medication use in the Test arm from Baseline to Month 12. By Month 12, the cohort of subjects taking opioids at baseline reduced its daily opioid utilization by over 60% from baseline.

- Overall non-opioid pain medication use declined from baseline to Month 3 in both treatment arms and continued with small further declines at Months 6 and 12.
- Pain interference to ADL showed a statistically significant decrease compared to baseline in both treatment arms at all follow-up timepoints, including in post-cross-over control subjects.
- There was a significant quality of life improvement for subjects in both treatment arms over the course of the study, as demonstrated by improvement variously in EQ-5D, SF-12 PCS, and SF-12 MCS.
- Based on PGIC, subjects in both treatment arms reported improvement at Months 6 and 12.
- Technical success, implantation and activation of the study device, was achieved in 97.3% of subjects.

Long Term Results

The responder rate was analyzed for the FAS population from Month 3 to Month 12. The Month 3-12 responder data in the crossed-over Control group reflects active Altius treatment in subjects who previously received active sham therapy. The purpose of this analysis was to assess both the durability of ongoing Altius treatment and the responder rate in Control subjects who crossed over to active treatment. In the FAS population comprising the Month 3-12 dataset (N=152), the responder rate was 30.1% (22/73) in the Test arm (12-months of active Altius treatment) and 15.2% (12/79) in the Control arm (9 months of active Altius treatment post Month-3) (**Table 11**:).

TABLE 11: RESPONDER RATE AT 30 MINUTES – MONTH 3 THROUGH MONTH 12, FAS POPULATION

	Test Group N = 73	**Control Group N = 79**	**Difference Test - Ctrl (95% CI)**	**One-sided p-value [1]**
Primary Performance Endpoint – Responders [2] [3] [4]	30.1% (22/73)	15.2% (12/79)	14.9% (1.8%, 28.1%)	0.206
95% CI	(19.6%, 40.7%)	(7.3%, 23.1%)		

[1] The responder rate was compared between treatment groups using logistic regression controlling for the following covariates: Etiology (dysvascular, trauma, other), Amputation Location (AKA, BKA), Pain Type (phantom, stump, both), Baseline Pain Intensity (5-6, 7-10) defined as the average of the end-of-day worst pain scores from the subject's e-diary compliant eligibility window, Baseline Pain Duration (episodic, persistent), and the Month 3 response outcome. Significance was evaluated using a one-sided test with alpha level 0.025.
[2] Subjects were considered a responder if they attained a significant pain reduction at the end of more than half of the treatment sessions subsequent to Month 3 through Month 12. Specifically, a responder must have attained ≥50% pain reduction in ≥50% of the treatment sessions during the Crossover phase of the study (Month 3 through Month 12).
[3] Missing pain score at 30 minutes for a particular completed treatment session was considered a failure for that session. Treatment sessions that were interrupted with rescue (p.r.n.) pain medications utilized the assessment of pain at the time of rescue medication, missing observations were considered a failure for that session.
[4] Subjects who were randomized to receive treatment but who terminated prior to their scheduled Month 12 Visit were determined to be a responder or non-responder based on their available data prior to termination.

Summary

In conclusion, the QUEST pivotal study met its primary safety and effectiveness endpoints and two of the secondary effectiveness endpoints for labeling. This study demonstrates that the Altius System is safe and effective for its intended purpose and has a favorable benefit/risk profile. The Altius System represents an important step forward in the treatment of post-amputation pain for a patient population, lower limb adult amputees, who are currently under-treated and in dire need of effective, non-addictive pain relief and the significant quality of life improvements that accrue from reducing or eliminating pain from their lives. Furthermore, the Altius System has the potential to address pain in a significant portion of the U.S. population that might otherwise use opiates and develop opioid addiction.

Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

3. Conclusions Drawn from Preclinical and Clinical Studies

3.1. Effectiveness Conclusions

Effectiveness for the Altius System was based on Level 1 evidence from the prospective multicenter randomized sham-controlled double-blind QUEST pivotal trial. One-hundred-eighty (180) subjects were implanted with the Altius System and randomized to active Altius stimulation therapy or sham-control (sub-therapeutic Altius stimulation); 170 subjects completed the Month 3 primary endpoint, 85 Test and 85 Control, and comprise the FAS population.

The QUEST study met its pre-specified primary effectiveness endpoint, demonstrating superior pain relief with the active Altius treatment (Test) compared to sham control, and the study was deemed a success with respect to effectiveness. The absolute difference between the treatment arms in terms of responder rate at Month 3 (i.e., treatment effect) was 17.6% in favor of active Altius treatment, and this difference was highly statistically significant.

Comparison between the Test and Control groups on three secondary effectiveness endpoints for labeling demonstrate the following clinical benefits of the Altius System:

- Greater reduction in opioid pain medication use at Month 3 by mean MED
- Greater reduction (improvement) in pain interference to ADL at Month 3 by mean BPI
- Greater improvement in quality of life at Month 3 as measured by SF-12 MCS

Additional multiple secondary effectiveness endpoints demonstrate the following clinical benefits in both Test and post-cross-over Control subjects:

- Continuing improvement in pain from baseline to Month 6 and Month 12 in both Test and Control
- Improvement in pain relief in both groups from 30 minutes to two hours post-Altius therapy at all timepoint
- Significant reduction in pain days per week in both groups at all timepoints, culminating at Month 12 in a reduction of approximately 3.5 pain days per week, >50% reduction in pain days compared to baseline
- Consistent significant decline in daily opioid and non-opioid pain medication use in both groups through Month 12
- Significant quality of life improvement in both treatment arms over the course of the study, as demonstrated by improvement variously in EQ-5D, SF-12 PCS, and SF-12 MCS

The benefits observed during the blinded study phase continued to increase through one year. Across all pre-specified primary and secondary endpoints, the 12-month data demonstrated that patients have reduced pain, reduce opioid medication consumption, and improved quality of life. In addition, improvements were observed between Month 3 and Month 12 on all primary and secondary effectiveness outcomes in the Control group following crossover to therapeutic treatment levels. All of these factors are crucial in evaluating the effectiveness of the Altius therapy.

3.2. Safety Conclusions

The risks of the device are based on nonclinical laboratory data and published literature as well as data collected in the QUEST clinical study conducted to support PMA approval as described above. SAEs related to the device occurred in 4.4% of the 180 patients implanted and randomized, and all SADEs resolved. No deaths attributed to the device or procedure occurred in the study. There were no unanticipated adverse device effects (UADE).

Regarding total SAEs throughout the study, the rates were similar in both study groups (41.4% of Test subjects vs. 42.9% of Control subjects) and 42.1% combined, in a study population with a high degree of co-morbidity and medical complexity. Implant site infection and/or wound complications occurred in 20% of subjects, most early in the study prior to the implementation of infection control mitigations; the infection rate was ≤5%% in the last 159 subjects enrolled, which is consistent with that of Spinal Cord Stimulation (SCS) devices.[1,2,3,4,5] Of all infection/wound complication events, 72% were minor and resolved without surgical intervention. Electrode cuff IS-1 connector failures occurred in 14.7% of FAS subjects; this issue was addressed with a design change and manufacturing improvements. Taking into account the infection mitigations and device deficiency resolution, the safety of the Altius System is similar to other approved implanted neuromodulation devices.

3.3. Patient Perspectives

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

3.4. Benefit-Risk Conclusions

The probable benefits of the device are based on the data collected in the QUEST pivotal clinical study described above. Effectiveness was demonstrated by improvement in pain at Month 3 with success of the primary effectiveness endpoint, as well as by improved pain interference to ADL and quality of life and significant reduction in opioid pain medication use. The benefits observed during the blinded Randomized Testing phase continued to increase through one year. Across all pre-specified endpoints, the 12-month data demonstrated that patients have reduced pain overall, reduced pain days per week, improved pain interference to ADL, improved quality of life, and reduced opioid and non-opioid pain medication use. In addition, the device -related SAE rate was 4.4% for both Test and Control groups combined and the risk of the device is similar to those of other active implantable systems such as SCS devices, despite the medical complexity of this patient population. In conclusion, therefore, given the available information cited above, the data support that, for relief of chronic PAP, the probable benefits of the Altius System outweigh the probable risks.

3.5. Overall Conclusions

The data in this application constitute valid scientific evidence within the meaning of 21 CFR 860.7, as the QUEST Study was well-controlled and well-design pivotal trial that met its primary safety and effectiveness endpoints. These data support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The data support the claims of post-amputation pain relief (pain reduction), reduced opioid medication use and improved quality of life.

4. References

ALTIUS SYSTEM CLINICAL SUMMARY

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