



## **RNS<sup>®</sup> System Patient Manual**

**For the RNS<sup>®</sup> Neurostimulator Model RNS-300M and Model RNS-320**

You should have two manuals, both this manual and the NeuroPace<sup>®</sup> Remote Monitor manual. Read both manuals before use. This manual is not meant to take the place of advice from your doctor. For a complete discussion of indications for use, contraindications, warnings, cautions, and potential side effects talk with your doctor.

**R<sub>X</sub>**Only

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DN 1019728 Rev. 2  
Rev. Date: 2023-10

## FCC Information

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The following is communications regulation information on the neurostimulator models RNS-300M and RNS-320, and wand model W-02.

- Neurostimulator model RNS-300M FCC ID: WBWRF300
- Neurostimulator model RNS-320 FCC ID: WBWRF320
- Wand FCC ID: WBW5200 or WBW902

These components comply with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) These devices may not cause harmful interference, and (2) these devices must accept any interference received, including interference that may cause undesired operation.

**Important:**

Changes or modifications to these components not expressly approved by NeuroPace, Inc. could void the FCC Certification, and negate your authority to operate them.

This equipment complies with FCC radiation exposure limits set forth for an uncontrolled environment. This transmitter must not be co-located or operating in conjunction with any other antenna or transmitter.

# Symbols

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Explanation of symbols on product or package labeling



Caution



MR Unsafe



MR Conditional



Prescription Only



Temperature limits during use



Temperature limits during storage or transport



Manufacturer



Serial number



Type BF applied part



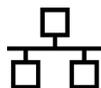
Class II electrical protection

5 V, 0.5 A

Direct current (DC) 5 V (volts), 0.5 A (amperes)

IP22

Ingress protection ratings: Level 2 for solid objects, which means testing confirms the device enclosure prevents ingress (entry) of items greater than 12.5 mm (~1/2 inch), such as fingers or similar objects; Level 2 for liquids, which means testing confirms vertically dripping water shall have no harmful effect when the enclosure is tilted at an angle up to 15° from its normal position.



Ethernet Connection (Network Connection)

Proposition 65, a State of California voter initiative, requires the following notice:



**WARNING:**

This product can expose you to chemicals including ethylene oxide, which is known to the State of California to cause cancer and birth defects or other reproductive harm. For more information go to [www.P65Warnings.ca.gov](http://www.P65Warnings.ca.gov).

**Note:** Images in this manual are representative and may vary in detail from what a particular user experiences.

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# About the RNS<sup>®</sup> System

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## INDICATIONS FOR USE

The RNS<sup>®</sup> System is an adjunctive therapy in reducing the frequency of seizures in individuals 18 years of age or older with partial onset seizures who have undergone diagnostic testing that localized no more than 2 epileptogenic foci, are refractory to two or more antiepileptic medications, and currently have frequent and disabling seizures (motor partial seizures, complex partial seizures and/or secondarily generalized seizures). The RNS<sup>®</sup> System has demonstrated safety and effectiveness in patients who average 3 or more disabling seizures per month over the three most recent months (with no month with fewer than two seizures), and has not been evaluated in patients with less frequent seizures.

## EPILEPSY AND ITS TREATMENT

Epilepsy is a brain disorder that causes seizures. Seizures occur when there is a sudden electrical misfiring of nerve cells in the brain. These misfires can cause convulsions or spasms, confusion, staring blankly, and sometimes loss of consciousness. There is no one cause of epilepsy. Genetics, head trauma, medical and developmental disorders may all play a role. Epilepsy affects nearly 3 million Americans and 50 million people worldwide.

Epilepsy is usually treated first with antiepileptic drugs. These drugs help to prevent seizures. If a person's epilepsy cannot be brought under control after trying two or more different antiepileptic drugs, that person's epilepsy is said to be medically refractory, i.e. the likelihood of achieving seizure freedom with another antiepileptic drug is less than 5%. If a person's epilepsy is said to be medically refractory the person may be a candidate for other treatments.

### Treatment with the RNS<sup>®</sup> System

The RNS<sup>®</sup> System is designed as a treatment for medical refractory partial epilepsy with partial onset seizures, in which seizures begin in a focus in the brain and then may spread to involve other parts or even the entire brain. The RNS<sup>®</sup> System does not treat other types of epilepsy (generalized epilepsies) in which seizures arise from all areas of the brain at the same time. People who use the RNS<sup>®</sup> System will continue to take antiepileptic drugs. Your doctor will know if you have the type of epilepsy and the kinds of seizures that can be treated with the RNS<sup>®</sup> System.

### Alternative Treatments for Medically Refractory Epilepsy

Epilepsy surgery involves removing or disconnecting the part of the brain that is triggering the seizures. Epilepsy surgery can be very helpful, but not all people with epilepsy are candidates for an epilepsy surgery that results in seizure freedom. Another treatment option for partial onset seizures is vagus nerve stimulation, which provides periodic electrical stimulation to the vagus nerve in the neck. In most cases, people who are treated with epilepsy surgery or vagus nerve stimulation continue to take antiepileptic drugs.

The type of treatment prescribed will depend on several factors. These include the frequency and severity of seizures, ability to localize seizure foci, the number of seizure foci, the person's age and overall health, and their medical history. An accurate diagnosis of the type of epilepsy is also critical to choosing the best treatment. The goal of all epilepsy treatment is to achieve seizure freedom or, if that is not possible, to control seizures, avoid the side effects of treatment, and make it possible for people to continue to lead lives that are not affected by seizures.

## DESCRIPTION OF THE RNS<sup>®</sup> SYSTEM

A small, battery-powered device (called a neurostimulator) is surgically implanted in the skull. Wires (called leads) that are connected to the neurostimulator are placed on and/or inside the brain. The neurostimulator monitors the electrical activity of the brain and detects abnormal activity that could lead to a seizure. If abnormal activity is detected, the neurostimulator delivers electrical stimulation to the brain through the leads to help prevent the seizure before it occurs.

The neurostimulator will be programmed for initial use by your doctor after it is surgically implanted. Then the neurostimulator settings will be adjusted on an ongoing basis as needed. The programmer lets your doctor do the initial programming and follow-up adjustments to the neurostimulator. Adjustments are based on brain activity and response to stimulation, which are both stored in the neurostimulator.

A remote monitor lets you collect data from the neurostimulator, and send the data to your doctor. The remote monitor consists of a special software program installed on a laptop or tablet computer, a wand and accessories.

After connecting the hand-held wand to the remote monitor, data in the neurostimulator are collected by placing the wand over the implant site. The wand uses Radio Frequency (RF) communication to collect the data. Data are stored in the remote monitor and then sent to a secure database over the internet. The database is called the PDMS (Patient Data Management System) and your doctor can access your data. Your doctor will review the data and use the results to adjust the neurostimulator settings during future office visits.

As part of the RNS<sup>®</sup> System, your doctor will provide you with a magnet. The magnet instructs the neurostimulator to record brain activity when you swipe it over the neurostimulator during a seizure. That way your doctor is able to identify the event during data review and make adjustments to the neurostimulator settings as needed. Another use of the magnet is to temporarily stop stimulation. (Your doctor may turn off this feature.) Although not expected to happen, you may want to stop stimulation if you think you are feeling the stimulation.

A medical implant identification card is provided that lets others know you are using the neurostimulator. Carry the card at all times. The card contains important information in the event you are being treated by another doctor who is unfamiliar with the RNS<sup>®</sup> System. You should also show this card before going through security systems at airports and other places. Refer to the [Warnings](#) on page 6 and [Cautions](#) on page 9 for specific information.

The neurostimulator remains implanted until your doctor determines that battery power is low. Then it is time to replace the neurostimulator. How long your battery lasts depends on the model of neurostimulator you have—which your doctor can tell you and is also on your Medical Implant Identification Card. For the model RNS-300M, this is usually after 2.6 to 4.3 years with typical use; for medium stimulation and detection settings the battery is estimated to last 3.9 years. For the model RNS-320, this is usually after 6.0 to 12.4 years with typical use; for medium stimulation and detection settings the battery is estimated to last 10.8 years. At that time, the neurostimulator is removed and a new one is implanted. Unless the leads need to be replaced, the new neurostimulator will be connected to the same leads.

## **RNS<sup>®</sup> SYSTEM PARTS**

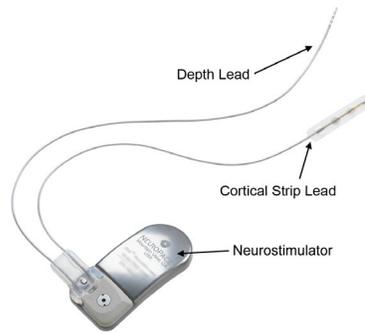
Read your **NeuroPace<sup>®</sup> Remote Monitor manual** for a description of your NeuroPace<sup>®</sup> Remote Monitor, wand, power cord, and accessories.

### **RNS<sup>®</sup> Neurostimulator**

The device implanted in the skull that delivers electrical stimulation.

### **NeuroPace<sup>®</sup> Cortical Strip Lead and NeuroPace<sup>®</sup> Depth Lead**

The leads are wires that connect the neurostimulator to areas of the brain where seizures start. The neurostimulator senses your brain activity and delivers electrical stimulation through these wires.



## **Magnet**

A device that lets you record brain activity during a seizure. The magnet also lets you temporarily stop stimulation (unless your doctor has turned off this feature).



## **Medical Implant Identification Card**

A wallet sized card that lets others know that you are using the RNS® System and makes them aware of procedures that may be harmful (such as an MRI), your physician's name and phone number, and which NeuroPace products have been implanted.

## **CONTRAINDICATIONS**

The RNS® System should not be used by people who:

- Are at high risk for surgical complications such as active systemic infection, coagulation disorders (such as the use of anti-thrombotic therapies) or platelet count below 50,000.
- Have another medical device implanted that delivers electrical energy to the brain.
- Are unable, or do not have the necessary assistance, to properly operate the NeuroPace® Remote Monitor or magnet.

DO NOT have any of the following medical procedures if you have the RNS® System implanted. These procedures produce energy that can travel through the neurostimulator and leads to the brain, and can result in brain injury or death. Turning the neurostimulator off prior to the procedure will not prevent problems from occurring. Even if the neurostimulator has been removed, problems can arise if any part of a lead is still implanted. If you have any of the procedures listed below while you have the RNS® System implanted, it may result in serious injury or possible death.

- Diathermy – High-frequency electromagnetic radiation, electric current or ultrasonic waves to induce heat in tissue anywhere on the body, either for therapy or relaxation. You absolutely CANNOT be treated with any type of shortwave, microwave, or therapeutic ultrasound diathermy device whether or not it is used to produce heat. These treatments should not be applied anywhere on the body.
- Electroconvulsive Therapy (ECT) – Electrically-induced seizures to treat psychiatric disorders.
- Transcranial Magnetic Stimulation (TMS) – Electromagnetic current to treat psychiatric disorders.

## Risks of Using the RNS<sup>®</sup> System

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There are benefits and risks associated with all medical devices and treatments. Talk to your doctor about the benefits and risks of the RNS<sup>®</sup> System and whether it is appropriate for you. Your doctor can also answer questions regarding the information in this manual.

### RISKS OF SURGERY AND TREATMENT

There are health risks associated with using the RNS<sup>®</sup> System. Risks include complications from surgically implanting the neurostimulator and leads. They also include potential risks related to the performance and use of the RNS<sup>®</sup> System. Discuss these risks with your doctor.

The risks of the surgery to implant the RNS<sup>®</sup> Neurostimulator and leads are comparable to other surgical procedures to treat epilepsy and to implant brain stimulators for Parkinson's disease. Risks associated with surgical implantation and treatment with the RNS<sup>®</sup> System include post-implant infection (7%) and bleeding in the brain or under the skull because of the implant (4.7%). There are also risks of infection and bleeding with surgery to replace or remove the neurostimulator and leads. There were other events which occurred during the studies which may or may not be related to treatment with the RNS<sup>®</sup> System. These included psychiatric symptoms (39.8%), changes in seizures (16%), and seizure related injury (49.2%), including seizure related head injury (10.5%). Eleven (11) patients died during the study. No patient died of a complication of a surgery related to the neurostimulator or leads. Patients with epilepsy, especially severe epilepsy, have a risk for sudden death (SUDEP). Seven (7) patients died from probable, possible or definite SUDEP, two patients died by suicide, one patient died of lymphoma, and one patient died of complications due to status epilepticus. Although some patients in the RNS<sup>®</sup> System studies died of SUDEP, there is no current indication that the risk of SUDEP in persons treated with the RNS<sup>®</sup> System is higher than expected for people with severe epilepsy.

Refer to [Clinical Studies: Risks and Benefits](#) on page 18 for more information.

The neurostimulator delivers electrical stimulation to the brain when it detects brain activity that your doctor feels could show the start of a seizure. You should not feel the stimulation but it is possible that you might feel a brief tingling sensation in your scalp or pain in your head. If you do, talk to your doctor so that changes can be made to the neurostimulator settings.

### NEUROSTIMULATOR/LEAD REPLACEMENTS AND FAILURES

For a full discussion of what to expect for the initial implant surgery refer to [Implant Surgery](#) on page 12. The model RNS-300M neurostimulator should work for about 2.6 to 4.3 years and the model RNS-320 neurostimulator should work for about 6.0 to 12.4 years with typical use before the battery power is drained. How long your battery lasts depends on which model of neurostimulator you have and the programming settings prescribed by your doctor. When the battery power gets very low, the neurostimulator will need to be surgically replaced with a new one. Your doctor will let you know when the neurostimulator needs to be replaced. The surgery involves first making an incision in your scalp. Then the surgeon will remove the old neurostimulator from its holder secured in the skull, and replace it with a new one. This surgery has less risk than the first surgery to implant the neurostimulator and leads because the doctor will not have to do any surgery on the bone and will not need to insert or move any of your leads. In many instances, this is done as an outpatient procedure and usually takes about one hour. As with any surgery, there are risks. During the clinical trials, some patients had pain at the incision site and infection after replacement.

If the RNS<sup>®</sup> System is not working properly, it may not provide the right amount of stimulation at the right time. If the neurostimulator is not working properly, you will need to have it replaced. If the leads are not working properly, then the neurosurgeon may suggest that the leads be changed. Sometimes, your doctor may want to change the leads that are connected to your neurostimulator. If these leads have already been implanted, the procedure is like the neurostimulator replacement and can be done as an outpatient procedure in an hour or less (compared with 2 to 5 hours for the first surgery). If new leads are inserted, then the procedure will be more like the initial implant surgery. Refer to [Clinical Studies: Risks and Benefits](#) on page 18 for more information.

You may not be aware of problems with the performance of the neurostimulator or leads unless you are having more frequent or more severe seizures than before. So it is important that you collect data from the neurostimulator and send data to the PDMS database as directed by your doctor. NeuroPace recommends you collect data from the neurostimulator at least once a day and, if you have a laptop remote monitor, send data to the PDMS database at least once a week. If you have a tablet remote monitor and it is connected to Wi-Fi as recommended, it sends data automatically after you collect it. If there is a concerning change in your seizures, you should also collect and send data to the PDMS database on a more frequent basis so that your doctor is able to decide whether any adjustments to the neurostimulator settings should be made. Refer to your remote monitor manual for more information.

People using the RNS® System will not be able to undergo certain medical procedures. These are procedures that might damage the neurostimulator/leads, or cause injury and even death. A list of these procedures can be found in [Contraindications](#) on page 3, [Warnings](#) on page 6, and [Cautions](#) on page 9.

## Warnings and Cautions

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### WARNINGS

#### **WARNING:** Medical Procedures

DO NOT have any of the following procedures before making sure the person administering the procedure knows that you have the RNS<sup>®</sup> System implanted and they have consulted with the doctor who is monitoring your use of the RNS<sup>®</sup> System:

- Computerized Tomography (CT or CAT) scans.
- Radiation therapy (such as cobalt 60 or gamma radiation to treat cancer).
- Lithotripsy (shock waves to break up hard masses, such as kidney stones).
- Electrolysis (electrical current to remove unwanted hair).

The energy used in these procedures may damage the RNS<sup>®</sup> System. This could result in stimulation not being delivered, additional surgery to remove or replace parts of the RNS<sup>®</sup> System, serious injury, or death.

In addition, Computerized Tomography (CT or CAT) scans should be performed only under the following conditions:

- The neurostimulator should be turned off prior to the procedure if possible. This should be done by your doctor or someone who is authorized to adjust the settings using the programmer.
- The scan should be taken at the lowest X-ray beam level possible.
- Avoid directing the beam at or near the implant site for more than a few seconds.
- Emergency services need to be available in the event you have a serious side effect. This is especially important if the scan area includes the implant site.
- The neurostimulator should be turned back on after the procedure.

Lithotripsy and Electrolysis should not be performed on the head or neck.

#### **WARNING:** MRI Safety Information



**RNS<sup>®</sup> Neurostimulator model RNS-320:** You must consult your doctor to determine whether an MRI scan is possible for you. The RNS<sup>®</sup> System (with RNS Neurostimulator model RNS-320) is MR Conditional, which means that an MRI scan may be safely performed under specific conditions. It may also be possible to have an MRI scan if your neurostimulator has been explanted. If your doctor determines it is possible for you to have an MRI scan, he or she must make sure that the conditions for a safe MRI scan are followed. Those conditions include putting your neurostimulator in MRI Mode, which uses more battery and may affect battery life. While in MRI Mode, the neurostimulator is not detecting or delivering therapy to the patient. Therefore, you should work with your doctor to minimize the time your neurostimulator is in MRI Mode.



**RNS<sup>®</sup> Neurostimulator model RNS-300M:** DO NOT have a Magnetic Resonance Imaging (MRI) scan if you have an RNS<sup>®</sup> System with an RNS Neurostimulator model RNS-300M implanted. The RNS Neurostimulator model RNS-300M is MR Unsafe. Having an MRI scan with an RNS Neurostimulator model RNS-300M implanted may result in serious injury or possible death.

**RNS<sup>®</sup> System External Components:** All external components such as the magnet, wand and remote monitor are MR Unsafe and can pose a projectile hazard, and therefore, must be kept out of the MRI scanner room.

Contact your doctor as soon as possible if you have questions or suspect your RNS<sup>®</sup> System is not working properly after any medical procedure.

**WARNING:** Interaction with Implanted Cardiac Devices

Possible effects of RNS<sup>®</sup> System interaction with an implanted cardiac device (such as pacemakers or defibrillators) include the following:

- Defibrillation therapy from an implanted defibrillator may damage the RNS<sup>®</sup> System.
- The electrical pulses from the RNS<sup>®</sup> System may interact with the sensing operation from a cardiac device and could result in an inappropriate response of the cardiac device and vice versa.

**WARNING:** Adverse Tissue Reaction

Allergic reaction to the RNS<sup>®</sup> System materials and/or leads implanted is possible.

**WARNING:** Chronic Tissue Stimulation

The effects of long-term brain stimulation are not completely known and may present some risks to the patient.

**WARNING:** Erosion

Skin erosion (breakdown of skin tissue) may occur on and/or around the neurostimulator and/or lead implant site, particularly in the case of protrusion of the implanted RNS<sup>®</sup> System products above the surface of the skull.

**WARNING:** Lead Migration

The implanted lead(s) may migrate (move) from their desired implant location. Lead migration can result in changes in detections and stimulation effectiveness, and may require additional surgical procedures to modify the lead location.

**WARNING:** Pregnant Women

The safety and effectiveness of the RNS<sup>®</sup> System has not been studied in pregnant women.

**WARNING:** RNS<sup>®</sup> System Failure

As with any electronic device, the RNS<sup>®</sup> System may malfunction (not work). Potential causes include battery malfunctions, an electrical short, open circuits, lead fractures, lead insulation failures, or damage as a result of head trauma. These malfunctions are unpredictable, and may result in too little stimulation or no stimulation. A lead failure may result in the lead needing to be removed or repositioned, which would require surgery. A malfunctioning neurostimulator may need to be replaced, which would require surgery. Although the device is designed to turn off if overstimulation or excess current occurs, there is a possibility that product failure could result in brain tissue damage.

**WARNING:** Case Damage

If the neurostimulator case is ruptured or pierced due to outside forces, severe brain tissue damage could result from exposure to the battery chemicals.

**WARNING:** Electrical Shock

To avoid electrical shock (as with any electronic device such as a laptop computer or tablet):

- DO NOT use the wand or remote monitor when you are wet.
- DO NOT apply water or liquids directly to the wand or remote monitor.
- DO NOT modify the power cord that came with your remote monitor in any way. If your remote monitor came with a 3-pronged plug, connect it to an outlet that accepts that type of plug.
- DO NOT use the wand or remote monitor during an electrical storm.
- DO NOT clean the wand or remote monitor with any cleaning liquids or aerosols. Wipe the outside of the wand and remote monitor with a clean cloth, dampened with water and wrung out. Make sure to disconnect the remote monitor from the electrical outlet before cleaning.
- DO NOT use the wand or remote monitor if you think they appear to be damaged or are not working properly.
- DO NOT attempt to modify or repair the wand or remote monitor. Contact NeuroPace Customer Support for assistance.

Not following these instructions may cause an electrical shock that may result in serious injury or death, and may damage the wand or remote monitor.

**WARNING:** NeuroPace® Equipment Placement

Use of NeuroPace® equipment (for example, remote monitor or programmer) adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, the NeuroPace® equipment and other equipment should be observed to verify that they are operating normally.

**WARNING:** Electromagnetic Interference (EMI)

Electromagnetic interference is a field of energy generated by equipment found in the home, work, medical, or public environments that is strong enough to interfere with neurostimulator function. Sources of strong electromagnetic interference can result in the following effects:

- Serious injury or death - It is possible for the interference sources to couple enough energy into a neurostimulator system to damage brain tissue.
- System damage - resulting in a loss or change in symptom control and requiring reoperation.
- Operational changes to the neurostimulator - causing stimulation to turn on or off, or resetting or reprogramming the neurostimulator resulting in a return of symptoms.
- Unexpected changes in stimulation - causing a momentary increase in stimulation which may be felt.

You should exercise caution to avoid devices which generate a strong electric or magnetic field. Refer to [Electromagnetic Emissions and Immunity](#) on page 24 for more information.

**WARNING:** Radio Frequency Identification (RFID) Interference

RFID scanners can produce signals that appear as brain activity to the neurostimulator. Such signals could cause the neurostimulator to deliver stimulation. Potential sources of RFID may occur in a health care environment, retail stores, public libraries, airports and business environments.

Refer to [Electromagnetic Emissions and Immunity](#) on page 24 for more information.

**WARNING:** Airport Security and Other Surveillance Systems

Tell people working with security and theft systems that you have the RNS® System implanted and show your medical implant identification card. Walk through the center of security screening units without stopping, when possible, and exit the area of the screening device as soon as possible. Leave the security area as soon as practical. Security screening devices (such as theft detectors, security tag deactivators, and airport security screening devices) may be found at retail stores, public libraries and airports. Such devices use technology that can cause or temporarily disrupt stimulation while you are being scanned. For more information, contact your local airport security office or TSA (Transportation Safety Administration).

**WARNING:** Laptop Overheating (applies to a laptop remote monitor)

DO NOT cover or enclose the laptop with anything that could restrict airflow through the vents and not allow heat to disperse. All laptop computers generate a moderate amount of heat when they are turned on. Restricting the airflow can damage the laptop or cause a fire.

**WARNING:** Wand Placement

DO NOT use (position) the wand over any other medical device. This includes other implanted devices such as a pacemaker or defibrillator, as well as devices that are used outside the body, such as a CPAP machine. Not following these instructions may momentarily interfere with the operation of other medical devices.

**WARNING:** Cables

Keep children from playing with the remote monitor power cord and wand cable, which can pose a risk of strangulation. To prevent damage to cables and the risk of electric shock, prevent pets, pests and children from chewing on cables.

## CAUTIONS

**Caution:** Medical Procedures and Dental Work

Before all medical procedures tell the person administering the procedure that you have the RNS® System implanted. All medical procedures and dental work should be performed with caution. Contact your doctor as soon as possible if you have questions or suspect your RNS® System is not working properly after a medical procedure.

Diagnostic x-rays and diagnostic ultrasounds may be performed without affecting the RNS® System.

**Caution:** Applying Pressure on the Neurostimulator and Leads

DO NOT press on or play with the implanted neurostimulator or leads. This may damage the neurostimulator or leads and result in stimulation not being delivered until they are surgically repaired or replaced.

**Caution:** Magnet

DO NOT drop the magnet onto any hard surface. The magnet can shatter into small, sharp pieces that can cut the skin.

**Caution:** Household Magnets and Magnetic Bracelets

DO NOT put items that contain magnets within 4 inches of the neurostimulator. Magnets contained in such products as stereo speakers, AM/FM radios, power tools, cellular, cordless and conventional phones, as well as magnets used therapeutically or worn on the body may interfere with stimulation. Since it is not always obvious if an item contains a magnet, refer to the packaging and instructions that came with the item for more information. You can also call the manufacturer of the item and ask them. Most headsets and earphones available in stores do not interfere with stimulation, but not all have been tested.

**Caution:** Battery Depletion

For continued operation, the neurostimulator needs to be surgically replaced when the battery is depleted. Your doctor will let you know when the neurostimulator needs to be replaced.

**Caution:** Neurostimulator Longevity

High and frequent levels of stimulation reduce neurostimulator battery longevity.

**Caution:** Removal and EMI Considerations

Before all medical procedures tell the person administering the procedure that you have the RNS® System implanted if any system components (neurostimulator, leads, lead fragments or cranial prosthesis) remain implanted after you stop using the RNS® System. You could still experience side effects from EMI if any system parts remain implanted. These effects may result in stimulation of the brain tissue and tissue damage resulting in serious injury or death.

Refer to [Electromagnetic Emissions and Immunity](#) on page 24 for more information.

**Caution:** Lead Replacement and Leads Left in Place

The long-term safety associated with leads left in place without use, replacement of leads, and lead removal is unknown.

**Caution:** Other Active Implanted Medical Devices

RNS® System interactions with other active implantable medical devices (such as pacemakers, defibrillators, implanted spinal cord and peripheral nerve stimulators, cochlear implants, and vagus nerve stimulators) are not known. Contact your doctor to discuss your situation or to answer questions.

**Caution:** Scuba Diving or Hyperbaric Chambers

DO NOT dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA). Such pressures could damage the RNS® System.

**Caution:** Patient Population for Which Safety and Efficacy Have Not Been Established

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

- People with generalized epilepsy
- People with a seizure focus that cannot be adequately localized
- Pregnant women
- Nursing mothers
- People under the age of 18
- People with simple partial sensory seizures only
- People with less than three seizures a month on average
- People who have more than two epileptic foci
- People who have not failed two antiepileptic drugs

**Caution:** Safety and Effectiveness Beyond 24 Months

The safety and effectiveness of the RNS® System beyond 24 months is unknown.

**Caution:** Remote Monitor Laptop or Tablet

DO NOT use the remote monitor laptop or tablet for any other purpose except as instructed. The laptop or tablet is designed to operate only as part of the remote monitor. DO NOT make any changes or adjustments to the remote monitor hardware or software. This includes attaching external devices like a mouse, or inserting CDs or DVDs into the drive. Any changes you make that are not part of the instructions may damage the remote monitor and may not allow you to send data to the PDMS database.

**Caution: Operating Temperatures**

DO NOT use the wand or remote monitor in temperatures above or below the recommended operating range (32°F -95°F). The wand or remote monitor may not operate properly at temperatures below 32°F or above 95°F. These devices may also become warm during normal operation. DO NOT use them when the room temperature is above 95°F to avoid discomfort.

**Caution: Remote Monitor Setup**

DO NOT set up the remote monitor where people can trip over the cords. The cords may be tripping hazards, especially for small children and pets. Tripping over the cords may damage the remote monitor parts, and may result in bodily injury. DO NOT rest anything on the power cord. DO NOT plug the wand into equipment other than the remote monitor because it could damage the wand. DO NOT use a USB cable extension from the remote monitor to the wand.

DO NOT move the remote monitor to another location without first disconnecting the parts and storing them in the carrying case. Disconnect the wand and all cords from the remote monitor. You may damage the parts if you do not disconnect them before moving them.

**Caution: Data Collection with a Tablet Remote Monitor**

You should collect data from the neurostimulator as directed by your doctor. If connected to a Wi-Fi network, the remote monitor sends data automatically to the PDMS database. NeuroPace recommends you collect data from the neurostimulator at least once a day and maintain a Wi-Fi connection to allow data to be sent to the PDMS database automatically. By receiving your data on a regular basis, your doctor will be able to identify problems and make adjustments. Your doctor will also be able to determine when battery power is getting low. If you do not collect data as directed, your doctor may not be able to review your data and make adjustments on a timely basis.

If you are having seizures more frequently or with greater severity, talk with your doctor as soon as possible. Your doctor may ask you to collect data on a more frequent basis until adjustments can be made to the neurostimulator settings.

Talk to your doctor about what you should do if you are unable to collect data from your neurostimulator as directed.

**Caution: Data Collection with a Laptop Remote Monitor**

You should collect data from the neurostimulator, and send data to the PDMS database, as directed by your doctor. NeuroPace recommends you collect data from the neurostimulator at least once a day and send data to the PDMS database at least once a week. By sending your data on a regular basis, your doctor will be able to identify problems and make adjustments. Your doctor will also be able to determine when battery power is getting low. If you do not collect and send data as directed, your doctor may not be able to review your data and make adjustments on a timely basis.

If you are having seizures more frequently or with greater severity, talk with your doctor as soon as possible. Your doctor may ask you to collect and send data to the PDMS database on a more frequent basis until adjustments can be made to the neurostimulator settings.

Talk to your doctor about what you should do if you are unable to collect data from your neurostimulator or send data to the PDMS database as directed.

**Caution: Wand Signal Test (applies to a laptop remote monitor only)**

DO NOT test the wand signal for more than 10 minutes a day. Testing the wand signal for more than 10 minutes a day may cause the neurostimulator battery to drain more quickly than expected.

**Caution: Remote Monitor Phone Line Use**

If you have a laptop remote monitor and are using a phone line to connect to the internet, you cannot make an outgoing call and send data at the same time, using the same phone number. If you need to make an emergency call while the remote monitor is sending data, disconnect the phone cord from the laptop. This will suspend data transmission so you can make the call. Any unsent data will be included with the data you

send the next time.

**Caution:** Analog Phone Line Required

If you have a laptop remote monitor and are using a phone line to connect to the internet, DO NOT connect your remote monitor laptop to any type of digital phone line such as phone systems used in many hotels and offices, phone service provided by cable companies, and VoIP (Voice over Internet Protocol). The remote monitor must be connected to an analog phone line. Connecting to a digital phone line will damage the laptop and not allow you to send data to the PDMS database. You will still be able to use the remote monitor to collect data from the neurostimulator.

# What to Expect with the RNS® System

## IMPLANT SURGERY

### Before Your Surgery

Your doctor will carefully examine you to locate the areas in your brain where your seizures start. This helps determine where the leads should be placed in the brain. Your doctor will also decide how many leads to implant, depending on the location of your seizures. The cortical strip lead is placed on the surface of the brain. The depth lead is placed inside the brain. Make sure your doctor explains all the risks associated with implant surgery, especially as they might relate to any other medical conditions you may have.

### Your Implant Surgery

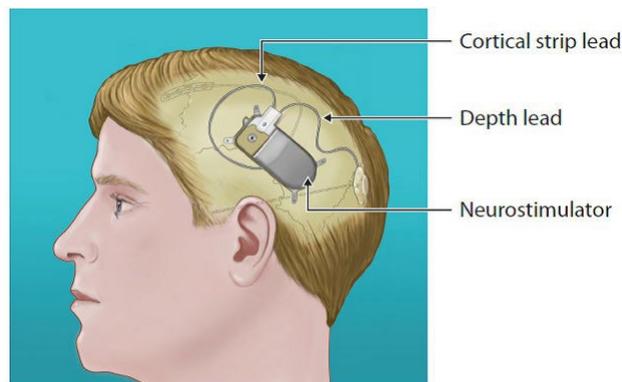
Your surgeon will determine what type of anesthesia you will need. You may be placed under general anesthesia for the neurostimulator implant.

The implantable RNS® System is made of two parts: the neurostimulator and leads (tiny wires with electrodes). The entire surgery should take approximately 2 to 5 hours.

During the procedure and while you are asleep, at least one cut, and maybe more, will be made in your scalp and skull (the exact places may vary). The cuts made for putting in the leads are about the size of a quarter, but may be larger. The cut in the skull for the neurostimulator will most often be made on the side toward the back of the head. The exact shape of the cut will be made to fit the neurostimulator. The position may be different depending on where the leads are placed and other factors. The neurostimulator is fixed in place and connected to two of the leads.

Usually two leads are implanted during the procedure. However, depending on the area where your seizures start, the doctors may decide that implanting up to four leads during the procedure may be the best option for you. No more than four leads will be implanted.

If you have more than two leads put in, only two leads will be connected to the neurostimulator. The ones that are not connected to the neurostimulator are not active and cannot deliver responsive stimulation. At a later time, the doctor may decide to change the leads connected to the neurostimulator, if needed. The inactive lead(s) could be attached to the neurostimulator and be made active during a second surgery. The surgery to connect a lead that is not active is not as major as the first surgery. Talk to your surgeon about the specific details of your surgery.



### Post-Surgery Recovery

You may remain in the hospital for a few days following surgery until your doctor feels it is okay for you to return home. Your doctor will also use that time to make sure there have been no complications from surgery and may program your neurostimulator for initial use. Your incision areas will be checked to make sure they are healing properly.

## Ongoing Treatment and Monitoring

The neurostimulator delivers electrical stimulation to the brain when it detects abnormal brain activity as determined by your doctor. You should not feel the stimulation. A few patients report that they feel the stimulation when first using the RNS® System. This side effect is usually resolved by your doctor making changes to the neurostimulator settings.

The RNS® System is designed to reduce the frequency of seizures. The majority of patients continue to experience seizures while using the RNS® System. You should expect to continue to take antiepileptic medications. Not everyone who uses the RNS® System will respond to stimulation the same way.

You will be expected to see your doctor for follow-up visits for as long as you use the RNS® System. The visits may be frequent at first and then not as often. At those visits, your doctor will adjust the neurostimulator settings based on data you have collected from the neurostimulator and sent to the PDMS database. You should talk to your doctor if you feel you are having seizures with greater frequency. It is a good idea to collect and send data to the PDMS database more frequently until your doctor is able to make adjustments.

Although the neurostimulator and leads are secured below your scalp, a blow to the head or neck may dislodge or damage them. If the parts move or are damaged, this may result in stimulation not being delivered until the neurostimulator or leads are surgically repaired or replaced. Talk to your doctor if you have had any type of head or neck trauma after you begin using the RNS® System. Although it is not known if there is a larger risk of bleeding in the brain after head trauma in patients who are implanted with the RNS® System, you should tell your doctor if you have any head trauma or injury to the head or neck.

## **THE NEUROPACE® REMOTE MONITOR AND WAND**

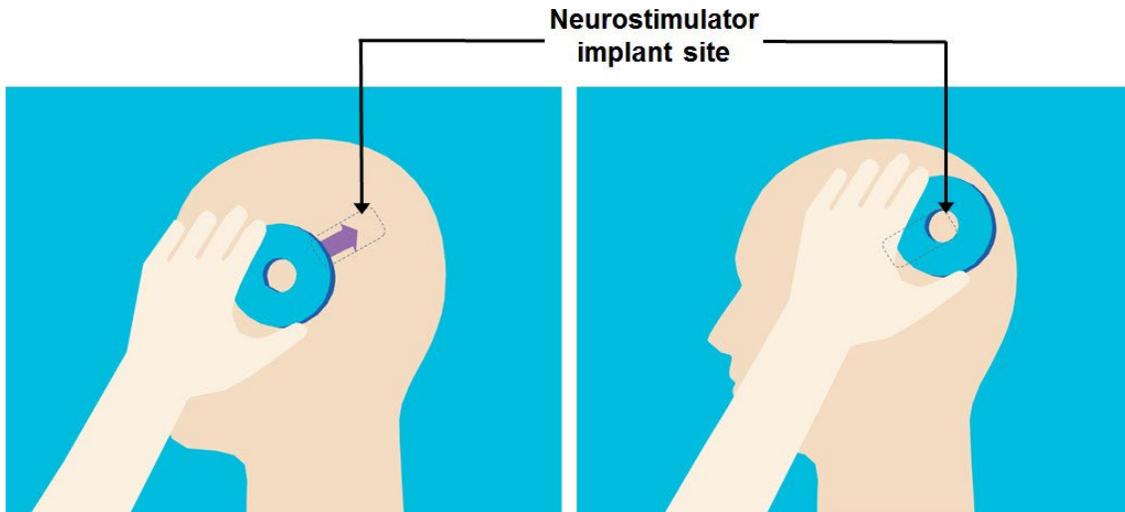
You will use the NeuroPace® Remote Monitor and wand to collect data from the neurostimulator and send the data to the PDMS database as directed by your doctor. NeuroPace recommends you collect data from the neurostimulator at least once a day and, if you have a laptop remote monitor, send data to the PDMS database at least once a week. If you have a tablet remote monitor and it is connected to Wi-Fi as recommended, it sends data automatically after you collect it.

The patient in the home is an intended operator of the remote monitor with wand. For complete instructions on the set up and use of the remote monitor and wand read your **NeuroPace® Remote Monitor Manual**. Contact NeuroPace Customer Support if you need assistance to set it up or to report any unexpected events.

## **THE MAGNET**

The magnet has two uses:

1. It instructs the neurostimulator to make a recording of your brain activity when you choose. To record an event, swipe the magnet over the neurostimulator while counting to 3. For example, swipe the magnet while you say “counting 1, counting 2, counting 3.”



Talk to your doctor to find out when you should use the magnet to record your brain activity (such as when a seizure is starting). The recording will be included with the other data you collect with the remote monitor and send to the PDMS database. At your next office visit, your doctor can review your brain activity and make adjustments to the neurostimulator settings as needed.

2. It lets you temporarily stop stimulation (unless your doctor has turned off this feature). You may want to do this if you feel the stimulation. To stop stimulation, hold the magnet in place over the neurostimulator. Stimulation will be stopped for as long as you hold the magnet in place. When you move the magnet away, normal operation will resume.



The only other way to stop stimulation is by your doctor adjusting the neurostimulator settings.

### WHEN IT'S TIME TO REPLACE THE NEUROSTIMULATOR

Your neurostimulator is powered by a battery and will need to be replaced when battery power is low. The model RNS-300M neurostimulator should last 2.6 to 4.3 years with typical use and the model RNS-320 neurostimulator should last 6.0 to 12.4 years with typical use. How long your battery lasts depends on which model of neurostimulator you have and the programming settings used by your doctor.

Your doctor will be able to determine when battery power is getting low. When the battery power gets very low, the neurostimulator can be surgically removed and replaced with a new one. Replacement surgery will be less complex and should take less time than when the neurostimulator was first implanted. Unless the

leads need to be replaced, the new neurostimulator will be connected to the same leads during the surgery. Your doctor may adjust the location of the leads at that time.

## Traveling with the RNS<sup>®</sup> System

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There are a few things you need to be aware of when traveling.

### **AIRPORT SECURITY**

#### **WARNING:** Airport Security and Other Surveillance Systems

Tell people working with security and theft systems that you have the RNS<sup>®</sup> System implanted and show your medical implant identification card. Walk through the center of security screening units without stopping, when possible, and exit the area of the screening device as soon as possible. Leave the security area as soon as practical. Security screening devices (such as theft detectors, security tag deactivators, and airport security screening devices) may be found at retail stores, public libraries and airports. Such devices use technology that can cause or temporarily disrupt stimulation while you are being scanned. For more information, contact your local airport security office or TSA (Transportation Safety Administration).

### **TRAVELING FOR AN EXTENDED PERIOD OF TIME WITHIN THE U.S.**

If you are unable to bring your remote monitor with you, you will not be able to transfer your neurostimulator data as directed. Talk with your doctor in advance to find out what you should do in these situations.

### **TRAVELING OUTSIDE THE U.S.**

The steps for connecting to the Internet from your remote monitor may be different outside the U.S. and you might not be able to connect or send data. Talk with your doctor in advance to find out what you should do in these situations.

## Care and Maintenance

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### NEUROSTIMULATOR AND LEADS

No special care and maintenance is required for the neurostimulator and leads.

### REMOTE MONITOR AND WAND

For information on the care and maintenance of your remote monitor and wand read your **NeuroPace® Remote Monitor Manual**.

## Clinical Studies: Risks and Benefits

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**Note:** There are risks and benefits associated with all medical devices and treatments. Talk to your doctor about the risks and benefits of the RNS® System and whether it is appropriate for you. Your doctor can also answer questions regarding the information in this manual.

The risks and benefits of the RNS® System were measured in three clinical studies. Patients participating in the studies were all adults who had partial onset seizures that began from 1 or 2 foci in the brain, and had frequent seizures that had not been controlled with at least 2 different antiepileptic medications. The first study was designed to show safety in 65 epilepsy patients who were being treated with the RNS® System for 2 years. The second study was designed to measure both the risks and benefits in 191 epilepsy patients being treated with the RNS® System and followed for 2 years. Following completion of one of the first two studies, patients had the option to enroll in the third long-term follow up study. During the third study, patients continued to receive stimulation and were followed for an additional 7 years to monitor long-term risks and benefits. Patients are still being followed in this long-term follow-up study. The first two clinical studies have been completed.

All of the studies looked at the risks of the RNS® System by measuring the number of adverse events. Adverse events included any complication or complaint that arose during the studies. Adverse events were measured for all patients throughout all of the studies.

In order to understand the benefits of the RNS® System, the second study had a 3 month comparison period. During the comparison period, half of the patients received stimulation (Treatment Group) and the other half did not (Control Group). Following the comparison period, all patients were able to receive stimulation for the rest of the time in the study. The studies measured benefits by looking at whether patients being treated with stimulation had fewer seizures. Patients completed daily seizure diaries and also filled out questionnaires about their seizure severity and quality of life.

### Risks

#### Safety Results

You can ask your doctor to discuss adverse events reported during the studies. Safety was assessed in all patients implanted with the RNS® System in all of the studies. Any event that occurred while a patient was participating in one of the studies at any time was reported as an adverse event, whether the doctor thought it was related to the RNS® System or not. This is customary in studies of new treatments.

In addition to reporting every adverse event, the investigator classified each adverse event as serious or non-serious and as device-related (which includes device-related and device relation uncertain) or not device-related. Adverse events were considered serious if they resulted in:

- Significant risk or impact on health
- Serious injury or death
- Hospital admission
- Surgery to stop or lessen the event

#### Pivotal Study

##### **SERIOUS ADVERSE EVENTS FOLLOWING SURGERY (PIVOTAL STUDY)**

The main goal of the Pivotal study was to compare the safety of the RNS® System to the safety of epilepsy surgery and to the safety of Deep Brain Stimulation for movement disorders. From implant to 4 weeks, the rate of serious adverse events with the RNS® System was 12.0% compared to 15% for epilepsy surgery. From implant to 12 weeks, the rate of serious adverse events was 18.3% for the RNS® System compared to 36% for the Deep Brain Stimulator. These results show that the safety of the RNS® System is comparable to these other procedures.

### ADVERSE EVENTS DURING THE COMPARISON PERIOD (PIVOTAL STUDY)

Serious adverse events were compared for the patients who were receiving stimulation during the Comparison Period (the Treatment Group) and for those who were not (the Control Group). There were 4 patients in the Treatment group (4.2%) and 5 in the Control Group (5.4%) who had serious adverse events. [Table 1](#) on page 20 presents the serious adverse events that occurred in these 9 patients.

During this same time period, non-serious adverse events occurred in 70 Treatment Group patients (72.9%) and 62 Control Group patients (66.7%). [Table 2](#) on page 21 lists the non-serious adverse events reported in 2.5% or more of the patients in either the Treatment or the Control Groups. This includes all adverse events whether the investigator felt they were device-related or not.

**Table 1: Pivotal Study - Serious Adverse Events During the Comparison Period**

Adverse Event	Treatment (N=96)	Control (N=93)
	% (#) patients with events	% (#) patients with events
Complex partial seizure increased	1.0% (1)	1.1% (1)
Alcohol poisoning	1.0% (1)	--
Hernia (hernia surgery)	--	1.1% (1)
Implant site infection due to seizure	--	1.1% (1)
Jaw fracture due to seizure	--	1.1% (1)
Myocardial infarction (heart attack)	1.0% (1)	--
Nephrolithiasis (kidney stone)	--	1.1% (1)
Pneumonia	1.0% (1)	--
Simple partial seizures (sensory)	--	1.1% (1)
Simple partial seizures increased (sensory)	--	1.1% (1)

**Table 2: Pivotal Study - Serious and Non-Serious Adverse Events in  $\geq 2.5\%$  of Patients in Either Group During the Comparison Period**

Adverse Event	Treatment (N=96)	Control (N=93)
	% (#) patients with events	% (#) patients with events
Nasopharyngitis (sore throat and runny nose)	6.3% (6)	8.6% (8)
Headache	5.2% (5)	7.5% (7)
Contusion due to seizure (bruise)	7.3% (7)	2.2% (2)
Skin laceration due to seizure (cut)	6.3% (6)	3.2% (3)
Complex partial seizures increased	4.2% (4)	3.2% (3)
Depression	5.2% (5)	2.2% (2)
Dysesthesia (painful sensation on the skin)	2.1% (2)	5.4% (5)
Influenza (flu)	4.2% (4)	3.2% (3)
Vomiting	3.1% (3)	3.2% (3)
Adverse drug reaction (bad reaction to medication)	3.1% (3)	2.2% (2)
Therapeutic agent toxicity (side effect of antiepileptic medications)	--	5.4% (5)
Upper respiratory tract infection (common cold)	1.0% (1)	4.3% (4)
Pain of skin	4.2% (4)	--
Pharyngitis (sore throat)	1.0% (1)	3.2% (3)
Abdominal pain	3.1% (3)	--
Balance disorder	--	3.2% (3)
Head injury	--	3.2% (3)

## COMBINED RNS<sup>®</sup> SYSTEM STUDIES

For the combined studies, all of the adverse events that occurred to any patient at any time were collected whether the doctor thought they were related to the RNS<sup>®</sup> System or not. Over the 903 patient years of experience, 64.5% (165/256) of the patients experienced a serious adverse event and 99.2% (254/256) of the patients experienced a non-serious adverse event, including common and expected illnesses and conditions, such as colds and flus. There were no unanticipated device-related serious adverse events in any of the RNS<sup>®</sup> System studies. Further detail is provided below.

### Deaths and SUDEP Analysis (Combined Studies)

Sudden unexpected death in epilepsy (SUDEP) is a term used when a person with epilepsy suddenly dies without a clear cause of death. The actual cause of SUDEP is unknown. There was a special committee of doctors who decided whether a death was because of SUDEP.

The information about deaths covers a longer period of time than for the other safety information. As of October 24, 2012, with over 1,195 patient years of treatment, 11 of the 256 patients in the RNS<sup>®</sup> System studies had died. One patient died of a cancer (lymphoma), one patient died of complications from status epilepticus (a seizure that lasts more than 30 minutes), 2 patients died by suicide and 7 deaths were linked to possible, probable or definite SUDEP. The number of SUDEP deaths that occurred during the RNS<sup>®</sup> System studies is comparable to what is expected in patients with severe epilepsy.

## **Device-Related Serious Adverse Events by Year (Combined Studies)**

Over the 903 patient years of experience, the most frequent device-related serious adverse events (occurring in  $\geq 2.5\%$  of patients) were implant site infection (5.9%), premature battery depletion (which required a surgical procedure) (4.3%), medical device removal (3.5%), and device lead damage (2.7%).

## **Serious Adverse Events of Particular Relevance (Combined Studies)**

Serious adverse events of particular relevance in persons with epilepsy and in persons with an implanted medical device include intracranial hemorrhage, infection, psychiatric events, change in seizures, status epilepticus and seizure-related injury. Serious adverse events in these categories for all patients in all RNS® System studies are discussed below.

### **INTRACRANIAL HEMORRHAGE**

Serious adverse events related to intracranial hemorrhage (bleeding in the brain or under the skull) occurred in 12 of the 256 implanted patients (4.7%):

- 4 were in the first 4 weeks after surgery.
- 3 were later than the first 4 weeks of surgery.
- 5 were due to a seizure-related head trauma.

2 patients (0.8%) had 2 non-serious adverse events because of an intracranial hemorrhage. These two events were considered non-serious because no medical treatment was required.

### **INFECTION**

Serious adverse events related to infections near the neurostimulator occurred in 18 of the 256 patients (7.0%):

- 1 was diagnosed before the RNS® System was implanted.
- 2 were due to seizure-related head trauma.

11 of the 18 (4.3%) patients had the neurostimulator and/or leads removed because of infection.

10 patients (3.9%) had 11 non-serious adverse events because of an infection. These were infections near the neurostimulator (5 patients, 2.0%) and at the incision site (6 patients, 2.3%).

### **PSYCHIATRIC ISSUES**

Many patients in these studies had a history of depression (49%) and/or suicidality (5.2%). Twenty-one of the 256 patients had a serious adverse event related to a psychiatric issue.

- 12 patients (4.7%) had 18 serious adverse events because of suicidality:
  - Suicide (2), depression with suicidal thoughts (6), suicide attempt (6), suicidal ideation (thoughts) (2) and suicidal behavior (threats or gestures) (2).
- 3 patients had a chronic psychosis.
- 2 patients had an acute psychosis.
- 2 patients had a conversion disorder (psychogenic seizures).
- 1 patient each had depression, psychosis after a seizure, emotional distress, affect lability (mood swings), agitation, alcohol abuse and alcohol withdrawal, and an episode of a visual hallucination.

81 patients (31.6%) had 148 non-serious adverse events because of a psychiatric issue. The most common were depression (47 patients, 18.4%), anxiety (21 patients, 8.2%) and depression with suicidal thoughts (4 patients, 1.6%).

### **CHANGES IN SEIZURES**

Some patients reported a serious adverse event because of more frequent seizures.

- 4 patients (1.6%) had more frequent simple partial motor seizures.
- 16 patients (6.3%) had more frequent complex partial seizure frequency.
- 15 patients (5.9%) had more frequent generalized tonic-clonic seizures.

Some patients reported a serious adverse event because of more severe seizures.

- 1 patient (0.4%) had more severe simple partial motor seizures.

- 15 patients (2.0%) had more severe complex partial seizure frequency.
- 11 patients (4.3%) had more severe generalized tonic-clonic seizures.

Three patients had a serious adverse event because of a new type (new symptoms) of a seizure.

Most of these were considered serious because the patient was admitted for video-EEG monitoring or hospitalized to modify antiepileptic medications.

109 patients (42.6%) had 361 non-serious adverse events because of a change in seizures. The most common were increased frequency of complex partial seizures (43 patients, 16.8%), new symptoms as part of a complex partial seizure (33 patients, 12.9%) and new symptoms as part of a simple partial sensory seizure (29 patients, 11.3%).

### **STATUS EPILEPTICUS**

Status epilepticus, commonly referred to as status, is a term used to describe a seizure that lasts 30 minutes or longer. Eight (8) of the 256 patients (3.1%) were hospitalized because of status epilepticus. One additional patient had status epilepticus after the neurostimulator and leads were removed, but while the patient was still in the study; the status occurred while the patient was being evaluated for epilepsy surgery with surgically implanted electrodes and had antiepileptic medications reduced.

1 patient had a non-serious adverse event because of status epilepticus. This patient was treated with oral medication as an outpatient.

### **SEIZURE-RELATED INJURY**

Twenty-three (23) of the 256 patients (9%) had a serious adverse event because of an injury that occurred during a seizure. Some patients had more than one type of injury:

- 7 patients had a laceration (cut).
- 5 patients fractured a bone.
- 4 patients had bleeding in the brain or under the skull.
- 3 patients were burned.
- 2 patients had a head injury.
- 2 patients developed an implant site infection after falling during a seizure.
- 1 patient had a joint injury.
- 1 patient had a contusion (bruise).

103 patients (40.2%) had 370 non-serious adverse events because of a seizure-related injury. The most common were contusions (bruises) (43 patients, 16.8%), lacerations (cuts) (38 patients, 14.8%), and head injury (25 patients, 9.8%).

### **Withdrawals and Discontinuations**

As of May 12, 2011, in the combined RNS® System studies, 43 of 256 (16.8%) patients stopped participating in the RNS® System studies. Seven (7) patients were explanted because of infection, 1 patient was explanted because of hemorrhage, 3 patients were lost to follow-up, 9 patients died and 23 patients withdrew by choice. As of October 24, 2012, 11 patients had died.

### **Neurostimulator Replacements**

There were 324 neurostimulators that were removed or replaced; 265 were replaced due to expected battery depletion. The usual amount of time until the neurostimulator was replaced because of expected battery depletion was 2.2 years.

Three (3) neurostimulators were replaced due to infection or erosion (skin breakdown). Eleven (11) neurostimulators were replaced during a procedure for lead revision. Eleven (11) neurostimulators were replaced due to premature battery depletion (this is discussed in detail below). One neurostimulator was replaced after a procedure to stop an unrelated cerebrospinal fluid leak. One neurostimulator was replaced because it was thought to be damaged after the patient was hit in the head. During a replacement procedure, one neurostimulator was not working and was replaced by another neurostimulator before the operative site was closed. No reasons were provided for 3 additional neurostimulator replacements.

Eleven (11) of the 256 patients had their neurostimulators replaced because the battery did not last as long as expected. These were batteries made by a certain manufacturer who no longer supplies batteries for the RNS® Neurostimulator.

There were 28 neurostimulator removal procedures. Thirteen (13) neurostimulators were removed due to infection (11) or scalp erosion (skin breakdown) at the incision site (2); two (2) were re-implanted at a later date. Other reasons for neurostimulator removal included epilepsy surgery (7), insufficient efficacy (3), to pursue other treatments (2), ongoing complaints (1), cerebral hemorrhage (1) and no reason provided (1).

Serious adverse events which occurred after the neurostimulator was removed included: 1 patient had a replacement of the bone at the implant site; 1 patient had worsening of tonic-clonic seizures (this patient later had the neurostimulator re-implanted); 1 patient had status epilepticus after the neurostimulator and leads were removed during evaluation for epilepsy surgery (this patient was already discussed).

### **Lead Damage, Removals and Revisions**

There were 11 procedures to replace or revise 14 damaged leads in 10 patients. During 9 of these procedures the damaged leads were replaced. During 2 of these procedures the damaged leads were disconnected and a previously implanted lead was connected to the neurostimulator.

There were 27 procedures to change the leads location for sensing and stimulation; 15 of these changes occurred during a routine neurostimulator replacement. Ten (10) patients had their leads revised when their neurostimulator was replaced. This was to: implant a new lead (4), connect a lead that was already implanted to the neurostimulator (4), replace a lead due to high impedance (1), and to replace leads after a procedure to stop an unrelated cerebrospinal fluid leak (1).

There were 24 procedures in which leads were removed or left behind at the same time that the neurostimulator was removed; 9 were due to infection, 7 were due to epilepsy surgery, 3 were due to insufficient efficacy, 2 were done to pursue other treatments, 1 was after a cerebral hemorrhage, 1 was as a result of ongoing complaints and 1 patient had no reason provided.

### **BENEFITS**

The RNS® System has been shown to reduce the frequency of disabling seizures in adults with partial onset seizures that have not been controlled with antiepileptic medications.

In the comparative study, seizure frequency was measured for 3 months in both the Treatment Group (received stimulation) and the Control Group (did not receive stimulation). The Treatment Group had a reduction in seizures of 37.9% and the Control Group had a reduction in seizures of 17.3%.

Seizure frequency was also measured by determining the number of patients who achieved a 50% reduction in seizures. During the 3 month Comparison Period 29% of patients in the Treatment Group and 27% of patients in the Control Group achieved a 50% or more reduction from baseline. There was no difference in the number of days without seizures and no difference in seizure severity between the Treatment and Control Groups.

After 1 year, almost half of the patients (44%) had at least 50% fewer seizures. And at 2 years, over half of the patients (55%) had at least 50% fewer seizures. Doctors could change antiepileptic medications after the Comparison Period (when all patients were receiving stimulation) as they thought was best for their patient. More than half of the patients did not have any medication changes (54%), 7.6% had their antiepileptic medications decreased, 22% had their antiepileptic medications increased and 16% had their medications both increased and decreased. Therefore, it is possible that some of the seizure reduction in some patients could have been due to changes in antiepileptic medications.

Quality of life (QOLIE) as measured by a questionnaire often used in epilepsy treatments was assessed. A significant clinical improvement on the QOLIE assessment is defined as an improvement of 5 points or more. 36.6% of patients in the Treatment Group and 39.1% of the patients in the Control Group had a significant clinical improvement at the end of the 3 month Comparison Period. At 1 and 2 years post-implant, 38% and 44% of patients (respectively) experienced a significant clinical improvement.

## Electromagnetic Emissions and Immunity

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 neurostimulator function. The RNS® System is designed to be immune from common sources of electromagnetic interference. The most common sources of EMI are discussed below. The warning regarding EMI on page 8 lists its possible effects.

The following table lists potential EMI sources found in hospital or medical environments that are contraindicated. DO NOT have any of the following medical procedures if you have the RNS® System implanted.

Item or procedure	Contraindicated
Diathermy treatment	X
Electroconvulsive therapy	X
Transcranial magnetic stimulation	X

You must consult your doctor to determine whether an MRI scan is possible for you, even if you have had an RNS neurostimulator explanted. Refer to MRI Safety Information on page 6 for more information.

For your convenience, the following tables list potential EMI sources alphabetically using these headings:

- Should not affect operation: Commonly used items that should not affect the operation of the neurostimulator.
- Avoid or exercise caution: You should avoid or exercise caution when in the presence of potential sources of EMI that may affect the operation of the neurostimulator system.

### HOSPITAL OR MEDICAL ENVIRONMENTS

You should always inform healthcare personnel that you have an implanted RNS® System (and show your medical implant identification card) before any procedure is performed. Most diagnostic procedures, such as x-rays and ultrasounds, may be performed without affecting the RNS® System. However other diagnostic and therapeutic equipment with higher energy levels may interfere with the RNS® System. Refer to [Warnings and Cautions](#) on page 6 for specific information.

Item or procedure	Should not affect operation	Avoid or exercise caution
Computerized tomography (CT or CAT) scans		See warning, page 6
Diagnostic ultrasound	X	
Diagnostic X-ray	X	
Electrolysis		See warning, page 6
Implanted cardiac devices		See warning, page 6
Lithotripsy		See warning, page 6
Medical procedures and dental work		See caution, page 9
Other active implanted medical devices		See caution, page 10
Radiation therapy		See warning, page 6
Removal and EMI considerations		See caution, page 10

## HOME, WORK, OR PUBLIC ENVIRONMENTS

Item or procedure	Should not affect operation	Avoid or exercise caution
Airport security and other surveillance systems		See warning, page 8
Appliances such as washing machines, dryers, electric stoves, toasters, blenders, electric can openers, and food processors	X	
Body fat measurement scales		X
Cell phones and Bluetooth devices	X	
Electric arc welding equipment		X
Electric blankets and heating pads	X	
Electric fences		X
Electric induction heaters		X
Electric steel furnaces		X
Electric substations, power generators, and large transformers		X
Electric toothbrushes, electric shavers, and hair trimmers	X	
Household magnets and magnetic bracelets		See caution, page 9
Jackhammers		X
Microwave ovens	X	
Personal computers, electric typewriters, copiers, and fax machines	X	
Portable and mobile RF communications equipment		X
Power lines and transmission towers		X
Radiofrequency identification (RFID) sources		See warning, page 8
Stun guns		X
Televisions, AM/FM radios, stereos, personal music players	X	
Vacuum cleaners and electric brooms	X	

For additional information about devices that generate electromagnetic interference contact NeuroPace. If you suspect EMI is disrupting the operation of your neurostimulator move away from the source of the EMI.

## **If You Need Help**

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If you are having a medical emergency call 911 and tell them that you have the RNS® System implanted.

### **CONTACT THE DOCTOR WHO MANAGES YOUR RNS® SYSTEM AS SOON AS POSSIBLE IF:**

- You are experiencing seizures with greater frequency or severity than before.
- You want to check if you can undergo a certain medical procedure or treatment while you have the RNS® System implanted.
- You are unable to collect and send data to the PDMS database as your doctor has directed.

### **CONTACT NEUROPACE CUSTOMER SUPPORT IF:**

- You need help with the set up or use of the remote monitor or wand.
- You need to replace any part of the remote monitor or wand.
- You need more information about what to do when traveling through airport security and other surveillance systems.

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