



THE RNS[®] SYSTEM

A patient's guide.





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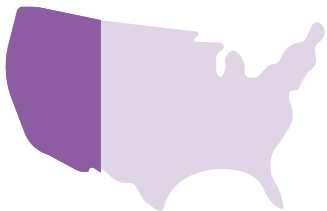
HOPE FOR DRUG-RESISTANT EPILEPSY

If you have tried at least two anti-seizure medications and still suffer from seizures, you may be among the more than 1,000,000 people in the United States living with drug-resistant epilepsy, also known as medically refractory epilepsy or hard-to-treat epilepsy. If medication alone is not working for you, there are other treatment options to consider:

- Resective or ablative procedures that remove or destroy brain tissue at the seizure source.
- Neuromodulation devices that use electrical stimulation to treat seizures.

Among neuromodulation devices, the RNS system is the only treatment that continuously monitors your brainwaves, recognizes and responds to your unique seizure fingerprint, and records EEG data for your doctor to review.

This guide provides you with in-depth information about brain responsive neurostimulation using the RNS® System.



>1,000,000

Americans experience seizures despite taking anti-seizure medications.¹



If you have tried two or more anti-seizure medications without achieving seizure control, there is less than a 5% chance that your seizures will be controlled on another medication."¹



Comprehensive Epilepsy Evaluation

Every person's seizures are different—with varying causes, seizure types, and symptoms. Choosing the best treatment option begins with understanding your seizures.

If you have drug-resistant epilepsy, you should consult an epilepsy specialist (also known as epileptologist) at a comprehensive epilepsy center (CEC). CECs have a team of experts who can provide complete evaluation and diagnostic testing, as well as extensive medical, device, and surgical treatment options.

Your CEC team might perform tests like the ones described on the next page.

EEG (Electroencephalogram)

An EEG shows the brain's electrical activity and is the most common test used to diagnose epilepsy. Electrodes are placed on your scalp to record the electrical activity of the brain. You may undergo 24-hour video EEG monitoring so doctors and nurses can monitor you while you are asleep and awake to record seizures.

CT (Computerized Tomography)

A CT scan is an X-ray that is taken from many angles and combined by a computer to create a 3-D image. CT scans can reveal brain abnormalities that might be causing the seizures, such as tumors, bleeding, and cysts.

MRI (Magnetic Resonance Imaging)

An MRI uses magnetic fields rather than X-rays to create a highly detailed image of your brain and its structures. An MRI may show subtle changes in certain brain areas that could be responsible for seizures.

Neuropsychological Testing

These tests are specifically designed to examine a variety of cognitive abilities such as how quickly you process information, your attention, memory, language, and executive functions. Neuropsychological testing helps determine treatment options, especially whether or not epilepsy resective surgery should be performed.

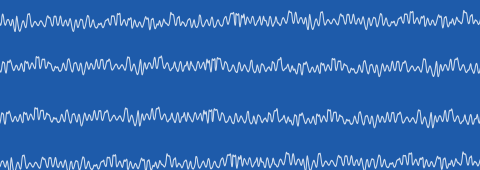
Intracranial Monitoring

If standard diagnostic tests do not pinpoint the source of your seizures, your epileptologist may decide that you need intracranial monitoring. Intracranial monitoring requires surgery to place electrodes over areas of your brain that may be generating your seizures followed by a period of video/EEG monitoring. This allows a much clearer recording than a scalp EEG.

Stereotactic electroencephalography (SEEG):

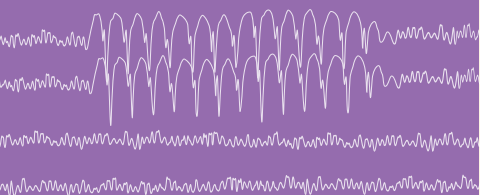
The SEEG is a minimally invasive diagnostic procedure that captures seizures with electrodes in the brain to get more detailed information on where seizures begin.

NORMAL EEG



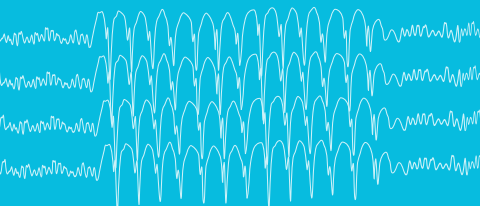
FOCAL SEIZURES

Start in one part of the brain



GENERALIZED ONSET SEIZURES

Involve the entire brain



UNDERSTANDING YOUR SEIZURES

Focal vs. Generalized Epilepsy

Seizures are generally described as either focal (partial onset) or generalized, based on where and how they begin. Individuals who have focal seizures may be candidates for resective surgery or neurostimulation therapies.

Focal (or partial onset) seizures

About two-thirds of drug-resistant patients have focal seizures that begin with an electrical discharge in one part of the brain. This is often referred to as the seizure focus. While it starts in one area, it can spread to or involve other areas of the brain (“secondarily generalized”).

Generalized onset seizures

About one-third of drug-resistant patients have generalized seizures that begin with widespread electrical discharge that involves the entire brain at once. Generalized onset seizures often have a genetic or hereditary cause.

Your Seizure Focus

The part of your brain where the seizures start is called the seizure focus. If you have focal seizures, your doctor may be able to identify your seizure focus by performing some of the tests described previously.

For some individuals whose seizure focus can be safely removed, resective surgery may be an effective treatment.

For individuals who have either two seizure foci or whose seizure focus is in an area that controls important functions such as memory, language, or motor function, resective surgery may not be an option.

In these cases, the RNS® System may be a good option. Like resective surgery, the RNS System treats your seizure focus. However, unlike resective surgery, it does this with electrical stimulation and does not involve removing any brain tissue.



Hippocampus or Mesial Temporal Lobe

The hippocampus is a structure that is deep in the brain and plays an important role in memory.



Frontal Lobe

This structure is associated with reasoning, planning, speech, movement, emotions, and problem solving.



Temporal Lobe

This structure is associated with movement, language, orientation, recognition, and perception of stimuli.



Parietal Lobe

This structure is associated with movement, orientation, recognition, and perception of stimuli.



Occipital Lobe

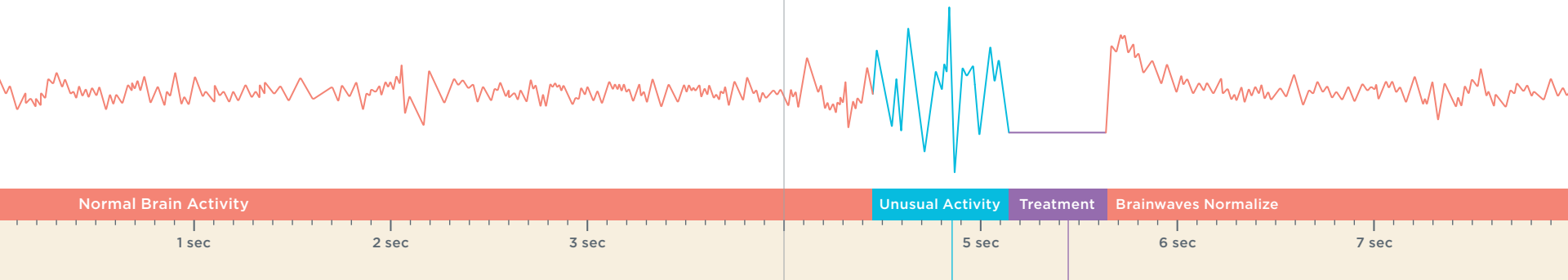
This structure is associated with visual processing.

Introducing the RNS System


The RNS System is a smart device that is designed to prevent seizures at their source. Similar to a pacemaker that monitors and responds to heart rhythms, the RNS System is the first and only medical device that can monitor and respond to brain activity. It is a complementary therapy to anti-seizure medications.


You may be a candidate for the RNS System if:


- You are 18 years of age or older
- You have frequent and disabling seizures
- You have tried two or more medications and still have seizures
- You have seizures that start in one or two areas of the brain



Here's how it works:

 **Monitors**
your brain activity 24 hours a day.

 **Recognizes & Responds**
to your specific seizure patterns.

 **Records**
EEG data for your doctor to review.

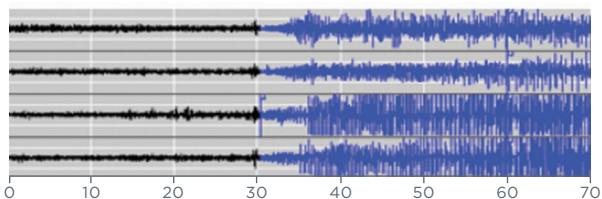
THE RNS® SYSTEM

Information about your brain activity

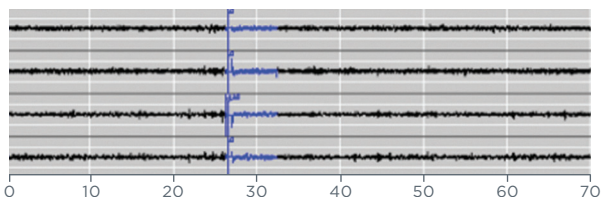
The RNS System records information about your brain activity over time. At home, you use a simple remote monitor to wirelessly collect information from the neurostimulator and

then transfer it to a secure website. Your doctor can log into the website at any time to review accurate information about your recorded brain activity and treatment progress. This information is private and made available to your medical team.

STIMULATION OFF: A recording from the neurostimulator shows unusual brain patterns that could lead to a seizure.



STIMULATION ON: Another recording from the neurostimulator shows the brain patterns returning to normal after stimulation has been delivered.



Seizure Reductions and Quality of Life Improvements

Effective seizure control

In a review study, patients treated with the RNS System experienced 82% median seizure reduction at 3 or more years.¹

In a 9-year clinical study, 1 in 4 patients experienced at least one seizure-free period of ≥ 6 months.²

Positive cognitive effects

Patients treated with the RNS System showed no evidence of cognitive decline. In fact, some demonstrated significant improvements in language and memory.³

Improved quality of life

Patients reported significant improvements in overall quality of life, including physical health, mental health, seizure worry, and cognition.⁴

No chronic stimulation side effects

The RNS System does not cause the chronic side effects associated with many anti-seizure medications such as

dizziness, drowsiness, depression, or confusion.⁵ It also does not have the ongoing stimulation-related side effects that can be associated with vagus nerve stimulation, such as hoarseness, shortness of breath, sore throat, and coughing.⁶

Risks

The primary risks associated with the RNS System are those related to most surgical procedures, such as risk of infection or bleeding. Consult with an epilepsy specialist about the full risks and benefits of the RNS System.

1. Razavi, et al. *Epilepsia*, 2020.
2. Nair, et al. *Neurology*, 2020.*relative to pre-specified comparator
3. Loring, D.W., et al. *Epilepsia*, 2015.
4. Meador, K.J., et al. *Epilepsy Behav*, 2015.
5. Heck, C.N., et al. *Epilepsia*, 2014.
6. Cyberonics. *Vagus Nerve Stimulation System Manual*. EO3 & EO5 Studies.



82% median seizure frequency reduction at three or more years.¹

How the RNS System is Different from Other Treatments

There are a number of features that distinguish the RNS System from other surgical options.

- **It monitors and treats the seizure source.** The RNS System constantly monitors your brain and directly stimulates your seizure focus.
- **It provides information about your brain activity.** The RNS System allows your doctor to see your brain activity while you go about your daily life.
- **It is a reversible therapy.** No brain tissue is removed. If you change your mind, the RNS System can be turned off and left in place. If desired, you can also have the device removed.
- **It is not noticeable.** After the RNS System procedure and proper programming by your doctor, you won't see the device or feel it working. Focus on your life—not your seizures.

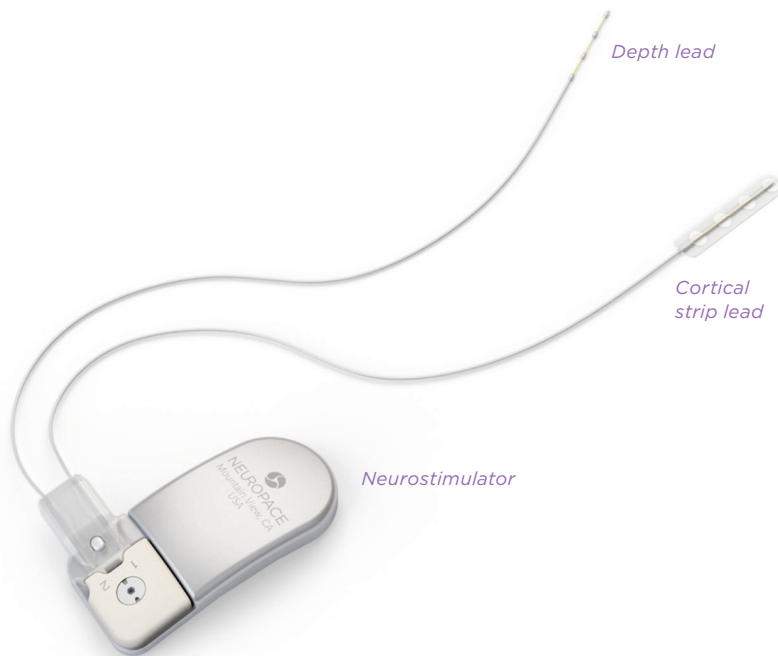
When Kim had the Vagus Nerve Stimulator put in, each time it went off, he could feel it. With the RNS System, his doctor programmed the device so he doesn't feel a thing when it's working—and his seizures have reduced by 77%.*



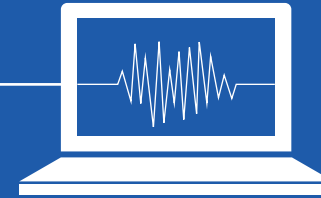
KIM L.

*Every person's seizures are different and individual results will vary.

RNS System Components



Wand



Remote Monitor



Magnet



ID Card

Neurostimulator

The neurostimulator is a small battery-powered device that is programmed by your doctor to deliver brief pulses of electrical stimulation to the brain when it detects unusual brain activity at the seizure focus. The neurostimulator is placed so that it is flush with the skull, and does not come in contact with your brain.

Leads

The leads are tiny wires that are implanted at the seizure focus or foci. Each lead has four electrodes that can be used for sensing and for stimulation. There are two types of leads, cortical strip leads and depth leads. Cortical strip leads are placed on the surface of the brain. Depth leads are placed within the brain.

Remote Monitor

A remote monitor lets you collect data from the neurostimulator, and send the data to your

doctor. The remote monitor consists of a laptop computer with a special software program, a wand, and accessories.

Magnet

The magnet is used to tell the neurostimulator to record brain activity when you are experiencing a seizure or seizure-like symptoms. It can also let you temporarily stop stimulation.

Medical Implant Identification Card

This wallet-sized card lets others know you are using the RNS System. It will also make them aware of procedures that are not allowed (such as any MRI if you have a model RNS-300M Neurostimulator; see Restricted Activities), your physician's name and phone number, and which NeuroPace product you have.

Procedure

The RNS System involves a surgical procedure that is performed by a trained neurosurgeon while you are under general anesthesia. Prior to the procedure, your medical team conducts testing to identify the location in your brain where your seizures start. During the procedure, your surgeon positions the lead(s) at the seizure focus or foci.

The next step is to place the neurostimulator in the skull and connect the leads to the neurostimulator (Figure A). A titanium tray is secured in the skull and the neurostimulator is then secured in the tray. Neither the tray nor the neurostimulator touches the brain. The neurostimulator is about as thick as your skull and curved—designed to be even with the skull surface. Once placed underneath the scalp, the device is not visible to you or anyone else (Figure B).

The neurostimulator is set up to begin detecting and recording

brain activity during the surgery. While in the hospital, you will be trained on how to use the remote monitor prior to discharge and will receive written instructions to take home. Most patients stay 1-2 nights in the hospital before going home. After returning home, you typically can resume normal activities. Your medical team, including your neurosurgeon, can describe the procedure in more detail, as well as the potential risks and benefits.

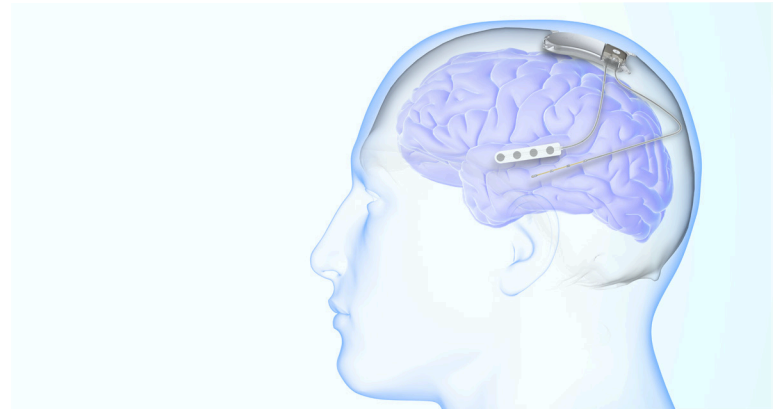


Figure A

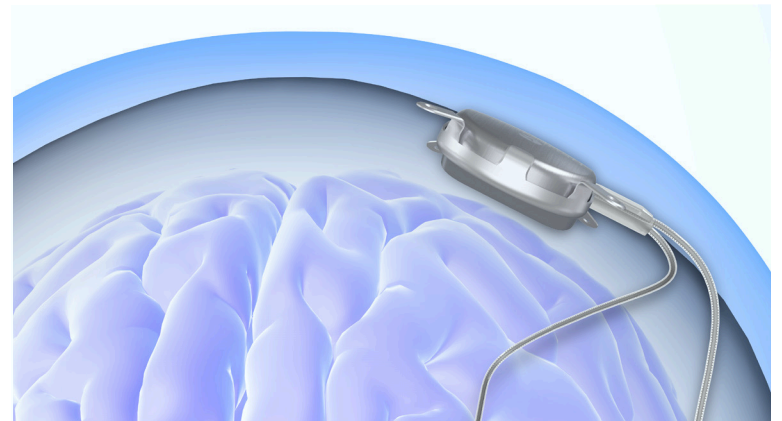


Figure B

Follow Up Visits

Initially, your doctor visits might be about once a month. Over time, your visits are likely to occur less often, usually every three to six months.

The follow-up visits allow your medical team to:

- Review your seizure diary and your seizure activity.
- Make any necessary adjustments to your neurostimulator.
- Discuss any questions or concerns you have.

Typically the stimulation function will be enabled at the first or second office visit after your brain activity has been collected by the neurostimulator. For as long as you use the RNS® System, you will need to see your doctor for follow-up visits.

Post-Procedure	Initial follow-up ~1 month	Subsequent visits ~every 3-6 months
<ul style="list-style-type: none"> • Your neurostimulator is programmed to monitor and detect brain activity. • You learn to use the remote monitor. • You typically return home after 1-2 days. 	<ul style="list-style-type: none"> • Your doctor reviews your seizure diary. • Your doctor reviews the data recorded by the RNS System. • Your doctor typically turns on stimulation at the first or second office visit. 	<ul style="list-style-type: none"> • Your doctor reviews your seizure diary. • Your doctor reviews the data recorded by the RNS System. • Your doctor adjusts device settings as needed.



Replacement Procedure

At medium stimulation and detection settings, the battery in the RNS-320 Neurostimulator is estimated to last nearly eleven years*, on average. Your doctor will let you know when the neurostimulator needs to be replaced.

During a replacement procedure, the surgeon will remove the old neurostimulator from the tray and replace it with a new one. Replacement procedures are typically outpatient procedures that last about an hour or less.

*The median battery longevity is 10.8 years for the RNS Neurostimulator (model RNS-320). Estimates for longevity were derived from medium stimulation and detection utilization (mAh/day).

Continue Your Normal Activities

In general, you should be able to continue your normal activities, such as:

- Traveling
- Exercising
- Using common household devices, including cell phones, computers, electronic tablets, most headsets and earphones, etc.
- Undergoing standard dental procedures such as X-rays, teeth cleaning and fillings (although you should not have procedures that involve electrocautery).

Share Data with Your Doctor

With the RNS System, you play an important role in managing your care. By collecting and sending information from your neurostimulator to a secure database you can help your doctor see your brain activity and ensure the device is working properly.

You will be trained on how to use the remote monitor (laptop, wand, accessories) prior to your discharge from the hospital. You will also receive written instructions to take home. Initially, NeuroPace recommends

that you collect data from the neurostimulator at least once a day and send data via the internet to the secure database at least once a week. Over time, you and your doctor will decide how often that should be.

Sharing data with your doctor usually takes about 5 minutes.



Step 1: Collect data from your neurostimulator

Place the wand over the neurostimulator and press a button on the laptop.

Step 2: Send data from your remote monitor to the PDMS

Ensure the laptop is connected to the internet and press a button.



Travel with the RNS System

You will not have any travel restrictions with the RNS System. But here are some things to keep in mind or consider.

- Airport scanners will not damage the system, but could cause or temporarily disrupt stimulation.
- You may want to inform the airport or security personnel that you have the RNS System by showing your Medical Implant Identification Card.
- You might want to bypass a body scan and opt for a pat-down security inspection.
- If you are unable to travel with your remote monitor, you won't be able to transfer your neurostimulator data. Talk with your doctor about your options.
- If you travel internationally, connecting to the internet might be different and you might be unable to send data. Talk with your doctor in advance to find out what you should do.

Restricted Activities

Once you have the RNS System, you should not undergo any of the following procedures.

Diathermy

You should not be treated with any type of shortwave, microwave, or therapeutic ultrasound diathermy device, whether or not it is used to produce heat.

Electroconvulsive Therapy (ECT)

You should not undergo any electrically-induced seizures to treat psychiatric disorders.

Transcranial Magnetic Stimulation (TMS)

You should not have any procedures that use electromagnetic currents to treat psychiatric disorders.

MRI

You cannot have an MRI if you have the RNS-300M model neurostimulator. The RNS-300M model is MRI Unsafe. FDA has approved MRI use for patients with the RNS-320 model neurostimulator and NeuroPace leads under certain MRI conditions. For more information, talk with your doctor and visit: www.neuropace.com/rns-system-mri-for-patients.

FREQUENTLY ASKED QUESTIONS

How quickly can I expect the RNS System to reduce my seizures?

Many people find that they experience a reduction in seizures when stimulation is started but it may take up to a year to optimize your neurostimulator settings. Every person's seizures are different and individual results will vary.

Can I expect to be seizure free?

Although you should not expect seizure freedom from the RNS® System, a subset of patients report experiencing seizure-free periods.¹

- In a clinical study, 1 in 3 patients experienced ≥90% seizure frequency reduction at 9 years.¹

Will I be able to stop taking my anti-seizure medications?

The RNS System is considered a complementary treatment to your medications. Your doctor will determine whether any of your medications should be changed.

Will stimulation be turned on right away?

Usually stimulation is turned on at the first or second office visit, about a month after the neurostimulator is implanted. The RNS® System will be programmed initially to gather data on your brain patterns. Once the RNS System has been personalized to detect your brain patterns, stimulation will be turned on and will automatically respond to unusual activity.

Will I feel the stimulation?

Once the therapeutic levels of stimulation are set, you should not feel any stimulation.

Does the effect of the RNS System wear off?

No. Experience over many years shows that seizure reductions appear to continue or improve over the long term.

Will people be able to see that I have the RNS System?

Once the RNS System is implanted underneath your scalp, it is not visible to you or anyone else.

Can the RNS System be removed if I change my mind?

If you change your mind, the RNS System can be turned off and you can have the device removed. But you don't need to. The neurostimulator and leads are designed so that they can be left in place even when no longer delivering therapy.

Will insurance cover the RNS System?

The RNS System is broadly covered by private and government insurance.

Can I speak to a patient who has the RNS System?

Yes, we can put you in touch with someone through our Patient Connections program. You can call **1-888-646-8483** or email connect@neuropace.com.

1. Nair DR, et al. *Neurology*, 2020.

Talk with your physician and see your Patient Manual and Remote Monitor Manual for additional information.

www.neuropace.com/product-manuals/

IMPORTANT SAFETY INFORMATION

Indication for Use

The RNS® 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® 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.

Contraindications

The RNS® System is contraindicated for patients at high risk for surgical complications, with medical devices implanted that deliver electrical energy to the brain, and those who are unable (or do not have the necessary assistance) to properly operate the NeuroPace® Remote Monitor or Magnet. For patients with an implanted RNS® System the following medical procedures are contraindicated:

- Electroconvulsive Therapy (ECT)
- Transcranial Magnetic Stimulation (TMS)
- Diathermy procedures (any treatment that uses high-frequency electromagnetic radiation, electric currents or ultrasonic waves to produce heat in body tissues)

Warnings and Precautions

The RNS® System is not compatible with non-NeuroPace leads and/or pulse generators. Electrical shock

may occur with incorrect use of the Programmer or Remote Monitor. Do Not Resterilize and Do Not Reuse the implantable products.

MRI Safety Information

RNS® Neurostimulator model RNS-320: An MRI scan may be safely performed on patients with the RNS® System (with RNS Neurostimulator model RNS-320) only under the specific conditions of safe use detailed in the MRI Guidelines for the RNS® System. Scanning under different conditions may result in device damage or malfunction and serious patient risks including permanent brain damage which may cause severe injury, coma, or death.

RNS® Neurostimulator model RNS-300M of the RNS® System is MR Unsafe. Having an MRI scan with a model RNS-300M Neurostimulator implanted may result in serious injury or possible death.

RNS® System External Components:

All external components and accessories of the RNS® System such as the Magnet, RNS® Tablet, NeuroPace® Programmer, NeuroPace® Remote Monitor, and Wand are MR Unsafe and can pose a projectile hazard in the MR environment, and therefore, must be kept out of the MRI scanner room.

Clinical Use

The RNS® System should only be implanted at Comprehensive Epilepsy Centers by neurosurgeons with adequate experience in the implantation of subdural and stereotactic implantation of intraparenchymal electrodes and in the surgical treatment of intractable epilepsy. The RNS® System should only be used by neurologists and neurosurgeons with adequate experience in the management of intractable epilepsy and in the

localization of epileptic foci. They must complete a NeuroPace® RNS® System training program and demonstrate specific expertise related to epilepsy, video-EEG monitoring, interpretation of electrocorticograms (ECoGs), the pharmacology of antiepileptic medications and selection of patients for epilepsy surgery. In some instances Neurologists who meet the experience and certification requirements but do not practice at Comprehensive Epilepsy Centers could be qualified by NeuroPace to provide post-implant programming.

Surgical

Implantation of the RNS® System and associated surgical procedure risks may cause, but are not limited to, infection, intracranial hemorrhage, tissue damage, temporary pain at the implant site, CSF leakage, seroma, and paralysis.

RNS® System and Therapy

The safety and effectiveness has not been studied in pregnant women. The effects of long-term brain stimulation are not completely known. Strong electromagnetic interferences (EMI) can result in serious patient injury or death, damaged brain tissue, loss or change in symptom control, reoperation, stimulation to turn on or off, a return of symptoms, or a momentary increase in stimulation felt by the patient. In addition EMI, such as security screening devices and radio frequency identification, can result in delivering the programmed stimulation to the patient and appear as sensing artifacts on the ECoG recordings. The RNS® System could interact with implanted cardiac devices and result in inappropriate device response or device damage. Additional surgical procedures can result from battery malfunction,

electrical short, open circuit, lead fracture, lead insulation failure, damage as a result of head trauma, or lead migration. Severe brain tissue damage can result from exposure to battery chemicals if the Neurostimulator is ruptured or pierced due to outside forces. The patient must collect data from the Neurostimulator once a day and send data to the PDMS once a week.

Medical Environment

Electrolysis on the head and neck should be avoided. Prior to the administration of Extracorporeal Shock Wave Lithotripsy or high radiation sources the administering physician should consult with the physician prescribing the RNS® System. Read the user manual to understand the steps to be taken before, during and after computerized tomography (CT) scans.

Potential Adverse Events

Serious adverse events occurring in ≥ 2.5% of patients and those of particular relevance reported during the RNS® System clinical studies include EEG monitoring, infection, change in seizures, medical device removal, death, device lead damage or revision, antiepileptic drug toxicity, hemorrhage, psychiatric events, status epilepticus and seizure-related injury. Refer to the product labeling for a detailed disclosure of other reported adverse events.

Rx Only. Refer to the product labeling for a detailed disclosure of specific indications, contraindications, warnings, precautions and adverse events.

DN 1014760 Rev 4
Rev. Date: 2020-03

We're here to help. And provide hope.

The RNS® System has provided many patients and their loved ones with an improved quality of life. If you are a candidate, there is a chance it can help you too. We encourage you to talk to an epilepsy specialist, an RNS Ambassador, or a NeuroPace Patient Educator.

For more information, please email connect@neuropace.com, call 1-888-646-8483 or visit [NeuroPace.com](https://www.NeuroPace.com).



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