



## Clinical Trials

***Note: The RNS® System Pivotal Clinical Investigation is closed to enrollment***

### Overview

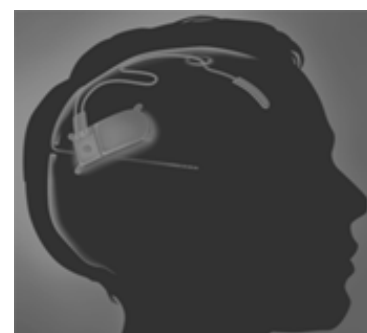
Epilepsy is a chronic neurological condition affecting over 2.5 million Americans of all ages. Despite treatment with antiepileptic medications, approximately 40-50% of people with epilepsy continue to experience seizures or have intolerable medication side effects. Epilepsy surgery may be an option for some individuals with refractory (hard to treat) epilepsy. However, many people cannot have surgery because it would be too risky and/or is unlikely to be helpful. Consequently, new therapies for epilepsy are needed. Brain devices to treat epilepsy are currently being studied and may offer hope to those persons with epilepsy who are not adequately treated by antiepileptic medication and are not candidates for epilepsy surgery.

### What is the purpose of the RNS® System Pivotal Clinical Investigation?

NeuroPace, Inc. is sponsoring an investigational device study of the RNS System, the company's responsive brain stimulation system for treating refractory epilepsy. The RNS System Pivotal Clinical Investigation is a randomized, double-blind, sham stimulation controlled investigation being conducted at approximately 31 sites throughout the United States. The purpose of the RNS System Pivotal Clinical Investigation is to assess the safety and to demonstrate that the RNS System is effective as an add-on (adjunctive) therapy in reducing the frequency of seizures in individuals 18 years of age or older with partial onset seizures (those that start from one or two areas of the brain) that are refractory (resistant or hard to treat) to two or more antiepileptic medications. Participants in the trial will continue to receive their epilepsy medications.

### What is the RNS System?

The RNS System is designed to detect abnormal electrical activity in the brain and to deliver small amounts of electrical stimulation to suppress seizures before there are any seizure symptoms. The RNS neurostimulator is placed within the skull and underneath the scalp by a surgeon. The neurostimulator is then connected to one or two wires containing electrodes that are placed within the brain or rest on the brain surface in the area of the seizure focus



(where seizures start). The RNS neurostimulator is designed to continuously monitor brain electrical activity from the electrodes and, after identifying the "signature" of a seizure's onset, deliver brief and mild electrical stimulation with the intention of suppressing the seizure. This type of treatment is called responsive stimulation, but it is not yet known if it will work for the treatment of epilepsy.

A modified laptop computer known as a programmer communicates with the RNS neurostimulator via a hand-held wand. The programmer collects information from the neurostimulator about brain electrical activity and is used to program the implanted device to make detections and deliver responsive stimulation.

### **How Long Does the Clinical Trial Last and How is the Study Designed?**

Study participation is expected to last approximately two to three years depending on when the eligibility criteria is met for implantation of the RNS System.

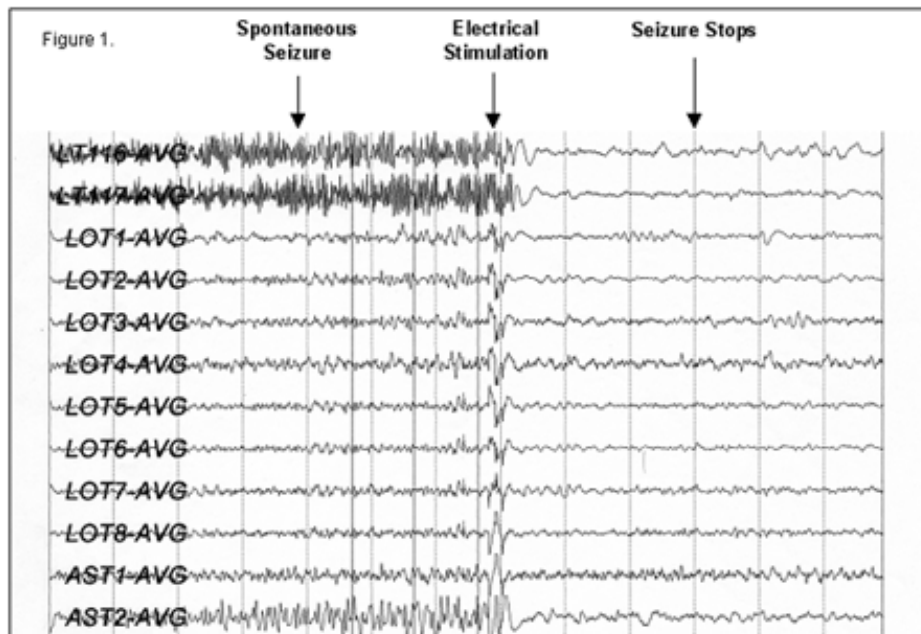
After enrolling in the study, participants first complete the baseline period, which lasts a minimum of three months and a maximum of 15 months. During this part of the study, participants will be given a seizure diary to keep track of their seizures on a daily basis. The doctor in charge of the study will review the frequency and severity of seizures during monthly telephone calls or office visits. Study participants must have an average of three seizures for three consecutive months to be eligible for implantation of the RNS System.

Once the eligibility criteria have been met, participants will be implanted with the RNS System. Study doctors will check on a participant's physical and emotional health and manage the implanted device during regularly scheduled follow-up visits. Participants will continue to keep a daily seizure diary.

The RNS System Pivotal Clinical Investigation is a randomized, double-blind, sham stimulation controlled investigation. The double-blinded portion of the trial begins 28 days after the RNS System is implanted and lasts about four months. Half of the participants will be randomly assigned (by chance) to have responsive stimulation turned ON and half will have responsive stimulation turned OFF (sham-stimulation). Participants and one doctor in the trial will not know whether stimulation is being delivered or not. Another doctor will program the RNS neurostimulator. Five months after the device has been implanted, when the double-blinded portion of the trial is completed, all participants will be able to have stimulation turned ON.

### **What Previous Clinical Research has been done with the RNS System?**

Previous research has shown that electrical stimulation of the brain can stop seizure activity. Here is an example of the brain's electrical activity showing the use of electrical stimulation to stop a seizure in someone's brain (Figure 1)\*.



\* Bergey, GB, et.al., Implementation of an external responsive neurostimulator system (eRNS) in patients with intractable epilepsy undergoing intracranial seizure monitoring. *Epilepsia* Vol 43, Suppl 7, 2002

### What are the Risks of Participating in the Clinical Trial?

Clinical trials involve risks. There may be side effects or adverse reactions to the device or therapy, or the therapy may make seizures worse. Implant of the RNS System requires brain surgery; as with any type of surgery there is risk involved. Any person involved in this study will be given an informed consent form that describes all known risks. As there is limited experience with the RNS System, there may also be other risks that are currently unknown. Prior to participation in a clinical study, it is always important to discuss the clinical trial procedures, risks, and potential benefits of any procedure or operation in more detail with the physician at the clinical trial site.

### Who is Eligible to Participate in the Clinical Trial?

Individuals who have been diagnosed with partial onset epilepsy (those that start from one or two areas of the brain) and have an average of three seizures per month that have not been controlled by taking two or more antiepileptic medications may be eligible to participate in this study. For more information about eligibility criteria, see the [Inclusion/Exclusion](#) criteria below or contact the closest participating center.

### Inclusion/Exclusion Criteria

#### Inclusion Criteria

1. Disabling motor simple partial seizures, complex partial seizures, and/or secondarily generalized seizures. Disabling refers to seizures that are severe enough to cause injuries, or significantly impair functional abilities in areas such as employment, psychological or social wellbeing, education or mobility.
2. Failed treatment with a minimum of two antiepileptic medications.
3. Experienced an average of three or more disabling motor simple partial seizures, complex partial seizures and/or secondarily generalized seizures every 28 days for three consecutive 28-day periods.
4. Between the ages of 18 and 70 years.
5. No more than two epileptogenic regions in the brain.

Note: Persons implanted with a vagus nerve stimulator (VNS) may be eligible

for the RNS trial if the VNS is turned off for a period of time and the person is willing to have the VNS generator explanted (excluding leads) prior to or at the time of the RNS implant.

### What should I do to find out more about the RNS Clinical Trial?

If you would like more information about the trial, you can contact a study center directly. You may also [contact](#) NeuroPace for more information about the trial and for contact information for other participating study centers. The personnel at a study center can explain the trial in detail.

A list of some of the participating study centers is provided below.

### Participating Institutions

The following is a partial list of sites participating in this study. You may [contact](#) NeuroPace for a complete list.

Institution	Location	Primary Contact	Epilepsy Center
University of Southern California	Los Angeles, CA	Sandra Oviedo (323) 442-5890	<a href="http://www.usc.edu/schools/medicine/departments/neurology/epilepsy/index.html">http://www.usc.edu/schools/medicine/departments/neurology/epilepsy/index.html</a>
California Pacific Medical Center	San Francisco, CA	David King-Stephens, MD (415) 600-7880 <a href="mailto:KingstD@sutterhealth.org">KingstD@sutterhealth.org</a>	<a href="http://www.cpmc.org/epilepsy/">http://www.cpmc.org/epilepsy/</a>
Yale University School of Medicine	New Haven, CT	Robert B. Duckrow, MD (203) 785-3865	
George Washington University	Washington, DC	James Leiphart, MD, PhD 202-741-2750	<a href="http://www.gwdocs.com/services/eHA-eHA_Content_C-Generic_Content_Page_Template_EpilepsyCenter.html">http://www.gwdocs.com/services/eHA-eHA_Content_C-Generic_Content_Page_Template_EpilepsyCenter.html</a>
Mayo Clinic - Jacksonville	Jacksonville, FL	Karey Doll, RN PhD (904) 953-6847 <a href="mailto:doll.karey@mayo.edu">doll.karey@mayo.edu</a>	<a href="http://www.mayoclinic.org/epilepsy/jaxtreatment.html">http://www.mayoclinic.org/epilepsy/jaxtreatment.html</a>
Georgia Health Sciences Institute	Augusta, GA	Patty Ray, PhD (706) 721-6260 <a href="mailto:PRAY@georgiahealth.edu">PRAY@georgiahealth.edu</a>	<a href="http://www.mcghealth.org/neuroscience-center/GhsuContentPage.aspx?nd=501">http://www.mcghealth.org/neuroscience-center/GhsuContentPage.aspx?nd=501</a>
Rush University Medical Center	Chicago, IL	Deborah Zielinski (312) 942-5939	<a href="http://www.rush.edu/rumc/page-1099611538227.html">http://www.rush.edu/rumc/page-1099611538227.html</a>
Indiana University	Indianapolis, IN	Marsha Manley, RNA (317) 274-0176 or (317) 274-0184	<a href="http://indianaepilepsy.services.iusm.iu.edu/iucomprehensiveepilepsycenter.htm">http://indianaepilepsy.services.iusm.iu.edu/iucomprehensiveepilepsycenter.htm</a>
Via Christi Comprehensive Epilepsy Center	Wichita, KS	Andrew Massey, MD or Toni Sadler, PA-C <a href="mailto:vcEpilepsyResearch@via-christi.org">vcEpilepsyResearch@via-christi.org</a>	<a href="http://www.via-christi.org/epilepsy">http://www.via-christi.org/epilepsy</a>
Massachusetts General Hospital	Boston, MA	Samantha Donovan (617) 643-4617	<a href="http://www.seizure.org/">http://www.seizure.org/</a>

Johns Hopkins University	Baltimore, MD	Gregory Bergey, MD (410) 955-7338 ext. 4 <a href="mailto:gbergey@jhmi.edu">gbergey@jhmi.edu</a>	<a href="http://www.neuro.jhmi.edu/epilepsy/">http://www.neuro.jhmi.edu/epilepsy/</a>
Henry Ford Hospital	Detroit, MI	Gregory Barkley, MD (313) 916-2451	<a href="http://www.henryfordhealth.org/body.cfm?id=45102">http://www.henryfordhealth.org/body.cfm?id=45102</a>
Mayo Clinic - Rochester	Rochester, MN	Karla Crockett (507) 284-2511 <a href="mailto:crockett.karla@mayo.edu">crockett.karla@mayo.edu</a>	<a href="http://www.mayoclinic.org/epilepsy/rst/treatment.html">http://www.mayoclinic.org/epilepsy/rst/treatment.html</a>
Dartmouth-Hitchcock Medical Center	Lebanon, NH	Barbara Jobst, MD (603) 650-6244 <a href="mailto:Barbara.Jobst@hitchcock.org">Barbara.Jobst@hitchcock.org</a>	<a href="http://www.dhmc.org/webpage.cfm?site_id=2&amp;org_id=128&amp;gsec_id=0&amp;sec_id=0&amp;item_id=3480">http://www.dhmc.org/webpage.cfm?site_id=2&amp;org_id=128&amp;gsec_id=0&amp;sec_id=0&amp;item_id=3480</a>
University of Rochester	Rochester, NY	Diane Smith (585) 275-0404 <a href="mailto:dianee_smith@urmc.rochester.edu">dianee_smith@urmc.rochester.edu</a>	<a href="http://www.stronghealth.com/services/neurology/epilepsy/index.cfm">www.stronghealth.com/services/neurology/epilepsy/index.cfm</a>
Oregon Health & Science University	Portland, OR	Rebecca Hoffenberg (503) 494-9633 <a href="mailto:hoffenbe@ohsu.edu">hoffenbe@ohsu.edu</a>	<a href="http://www.ohsu.edu/epilepsy">http://www.ohsu.edu/epilepsy</a>
Baylor College of Medicine	Houston, TX	Eli M. Mizrahi, MD (713) 798-0980 <a href="mailto:emizrahi@bcm.tmc.edu">emizrahi@bcm.tmc.edu</a>	<a href="http://www.BaylorEpilepsyCenter.org">http://www.BaylorEpilepsyCenter.org</a>
University of Virginia	Charlottesville, VA	Stacy R. Thompson, RN, BSN, CCRC (434) 982-4315 <a href="mailto:SRC2H@hscmail.mcc.virginia.edu">SRC2H@hscmail.mcc.virginia.edu</a>	
Swedish Medical Center	Seattle, WA	Epilepsy Center Research Project Coordinator (206) 320-2261 or (206) 215-3565	<a href="http://www.swedish.org/body.cfm?id=158">http://www.swedish.org/body.cfm?id=158</a>
University of Wisconsin School of Medicine and Public Health	Madison, WI	Talley Mitchell (608) 263-1739 <a href="mailto:tmmitchell@clinicaltrials.wisc.edu">tmmitchell@clinicaltrials.wisc.edu</a>	<a href="http://www.neurology.wisc.edu">http://www.neurology.wisc.edu</a>

Caution: The RNS system is an Investigational device. Limited by United States law to investigational use.

To learn more about clinical trials, visit:

- [ClinicalTrials.gov](http://ClinicalTrials.gov)
- [U.S. Food and Drug Administration](http://www.fda.gov)

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