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JNS PEDIATRICS

CLINICAL ARTICLE

Responsive neurostimulation device therapy in pediatric patients with complex medically refractory epilepsy

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OBJECTIVE Pediatric epilepsy is characterized as drug resistant in 20%–30% of patients and defined as persistent seizures despite adequate treatment with two first-line antiepileptic medications. The American Academy of Neurology advocates surgical options earlier in the treatment of epilepsy to provide long-term seizure reduction. The new development of minimally invasive approaches has recently allowed for surgical options to patients not previously deemed surgical candidates. These may include patients with bilateral, deep, eloquent, or poorly localizing epileptogenic foci. To this end, responsive neurostimulation (RNS) is an FDA-approved closed-loop neuromodulation device for adjuvant treatment of adults with medically intractable epilepsy arising from one or multiple foci.

METHODS In this study, the authors describe their initial institutional experience with the use of RNS in pediatric patients with drug-resistant epilepsy. An IRB-approved retrospective review was conducted of 8 pediatric patients who underwent RNS implantation at Cincinnati Children's Hospital Medical Center between 2019 and 2021.

RESULTS Eight patients met the inclusion criteria for the study. The average age at the time of surgery was 14.7 years (range 8–18 years) with a mean follow-up of 16.5 months. All patients underwent invasive monitoring with stereo-EEG, subdural grid placement, or a combination of both. All patients had either bilateral or eloquent cortex targets. Trajectories were based on noninvasive (phase 1) and invasive (phase 2) seizure onset zone localization data. Four (50%) of the 8 patients underwent surgical intervention for epilepsy prior to RNS placement. RNS electrodes were placed with robot-assisted guidance in a hybrid operating room with intraoperative CT and electrocorticography. The authors demonstrated individualized RNS electrode trajectory and placement with targets in the amygdala/hippocampus, bilateral insula, bilateral parietal and occipital targets, and frontoparietal regions for a total of 14 implanted electrodes. One adverse event occurred, a wound infection requiring return to the operating room for removal of the RNS implant. All patients demonstrated a reduction in seizure frequency. All patients achieved > 50% reduction in seizure frequency at last follow-up.

CONCLUSIONS RNS implantation in carefully selected pediatric patients appears safe and efficacious in reducing seizure burden with a low rate of operative complications.

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KEYWORDS responsive neurostimulation; epilepsy; pediatric seizures; RNS; neuromodulation

Medically refractory epilepsy, defined as persistent seizures despite two first-line antiepileptic medications, is prevalent in 20%–30% of pediatric epilepsy patients.[1] The latest guidelines from the American Academy of Neurology now advocate for early consideration of surgical options to provide long-term seizure reduction more effectively and expeditiously.[2] The development of minimally invasive surgical approaches allows options for patients who were previously not considered to be surgical candidates, particularly those with bilateral, deep, eloquent, or poorly localizing epileptogenic foci. Particularly for patients with anatomical overlap between driver nodes of seizure-generating network and functional nodes, neuromodulation has emerged as a viable option.

ABBREVIATIONS fMRI = functional MRI; RNS = responsive neurostimulation; SDG = subdural grid; SEEG = stereo-EEG.

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Responsive neurostimulation (RNS) is an FDA-approved closed-loop neuromodulation device for treatment of medically refractory epilepsy (RNS System, NeuroPace, Inc.). Neurostimulation is the term used to describe the application of electricity to the CNS with the goal of reducing seizure frequency and severity. A closed-loop system senses brain activity based on a predefined seizure-detection algorithm and delivers stimulation based on detected events to abort seizures.[3] Heck et al. demonstrated the safety and efficacy of RNS as an adjunct therapy to reduce the frequency of seizures in adults with medically intractable epilepsy as part of a multicenter, double-blinded, sham-stimulation controlled pivotal study.[4] Although RNS was initially conceived to abort seizure activity, it may also have long-term beneficial effects by altering the plasticity of relevant neuronal networks. There is evidence that RNS response is due to indirect prevention rather than through directed triggered seizure inhibition.[5] RNS is currently FDA approved for adults 18 years of age or older. However, recent case reports have described the off-label application of RNS in pediatric patients.[6,7] In this study, we report our institutional experience using RNS for various etiologies of medically refractory epilepsy in a complex pediatric population.

Methods

An IRB-approved retrospective review of pediatric patients who underwent RNS implantation at Cincinnati Children's Hospital between 2019 and 2021 was conducted. Each patient was reviewed by the multidisciplinary surgical epilepsy team at Cincinnati Children's Hospital prior to consideration of RNS as a treatment option for medically refractory epilepsy. Briefly, if patients are deemed to have intractable epilepsy by our neurology epilepsy team, they undergo noninvasive monitoring and testing over a 5-day period that may include video-EEG, MRI of the brain, PET, SPECT/SISCOM (subtraction ictal SPECT coregistered with MRI), magnetoencephalography, and functional MRI (fMRI) as indicated. After discussion of results at a comprehensive epilepsy surgery conference, a decision is made for next appropriate management course.

The following variables were collected: age, sex, age at epilepsy onset, etiology, comorbidities, preoperative seizure frequency, fMRI findings, seizure onset zone, history of previous surgery, stereo-EEG (SEEG) findings, subdural grid (SDG) placement details and results, localization, target of implantation, surgical technique, complications, follow-up, postoperative seizure frequency, and calculation of reduction in seizure frequency (Table 1).

Seizure frequency reduction was based on preoperative seizure frequency and postoperative seizure frequency recorded in the electronic medical record. Baseline seizure frequency was reported at the most recent 3-month interval leading to an office visit prior to RNS implantation. Postoperatively, patients were seen at 1 month for initial programming and were followed at regular 3-month intervals for reprogramming. Patients were encouraged to use an online seizure diary and to mark seizures by swiping the provided magnet over the generator whenever possible. Seizure outcome was recorded as seizure frequency as reported by the patient or their family over the most recent 3-month interval. This measure was compared with baseline seizure frequency to generate a result for percentage reduction. For patients with multiple seizure types, the most disabling (typically convulsive) seizure was represented for seizure outcome. Additionally, we reviewed RNS parameters as established by the neurology team (Table 2).

Selection of RNS Targets

Localization of the seizure foci and RNS targets was based on noninvasive data from the phase 1 evaluation and phase 2 evaluation data from intracranial SDG or SEEG monitoring in all patients. Figure 1 demonstrates patient 3 as a patient with different modalities used for localization and treatment. Two patients underwent right-sided SEEG, 2 underwent left-sided SEEG, 5 underwent bilateral SEEG, and 2 patients underwent SDG placement for invasive monitoring (Table 1). The average number of depth electrodes placed for SEEG was 13.4 (range 5–16 and a range of 44–192 contacts), while the 2 patients undergoing SDG placement had an average of 78 (64 and 92) cortical contacts. Implantation times ranged between 3 and 13 days for all invasive monitoring procedures. No surgical complications were recorded as a result of invasive monitoring. Four patients were identified as having bilateral seizure onset zones. Seven patients had at least one eloquent cortex target, including 1 patient who demonstrated right-sided language localization on fMRI and electrode stimulation during SEEG (patient 1). Individualized robot-guided stereotactic electrode trajectories and targets were planned to diverse anatomical locations, including the amygdala/hippocampus, bilateral insula, bilateral parietal and occipital targets, and a frontoparietal region for a total of 14 electrodes implanted (Tables 1 and 2).

Surgical Technique

Patients were tested for methicillin-resistant *Staphylococcus aureus* colonization prior to surgery and underwent a decolonization protocol if positive. If methicillin-resistant *S. aureus* results were positive, the antibiotic regimen included vancomycin in addition to cefazolin for 24 hours postoperatively. Under normal circumstances, we administered a weight-based dose of cefazolin intraoperatively prior to incision. Patients were then given 3 doses of cefazolin postoperatively. We used a protocol with total intravenous anesthesia, including a paralytic because of the need for intraoperative electrocorticography recordings from the RNS device. Patients were administered antiepileptic medications prior to surgery to prevent intraoperative epileptic events. Intravenous steroids were given at the time of the first electrode placement. While passing the electrodes, systolic blood pressure was monitored using an arterial line and maintained at or slightly below normotension for age. In general, a radiolucent three-point fixation head clamp was used for unilateral targets and a CRW stereotactic head frame was used for bilateral targets. At our institution, we use the ROSA (Robotic Surgical Assistant) robot (Zimmer Biomet) for stereotactic guidance. The incision was planned to accommodate placement of

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TABLE 1. Patient cohort demographic data

Pt No.	Age (yrs), Sex	Etiology of Epilepsy	Comorbidities	No. of AEDs	SEEG/SDG Laterality	No. of DEs/ Contacts	Implantation Time Duration (days)	Complications from SEEG/ SDG	Pre-RNS Sz Focus Intervention	Preop Sz Frequency	Targets	No. of DEs	FU From RNS Implant (mos)	Postop Sz Frequency
1	14, M	PRES	Nephrotic syndrome	2	Rt SEEG	8	3	N	None	8/mo	Rt amygdalo-hippocampus	1	39	2/mo
2	8, M	Chromosomal abnormality	ASD, VSD, coarctation of aorta (s/p repairs), IVH/hydrocephalus (s/p VP shunt), ADHD, tracheomalacia, vocal cord paralysis, hydro-nephrosis	4	Rt SEEG Bilat SEEG	12 8	3	N	Rt AH LITT	6/mo	Lt amygdalohip-pocampus	1	17	1/mo
3	16, F	Hypoglycemic insult	Severe hypoglycemia due to hyperinsulin-ism (50% Roux-en-Y pancreatectomy); islet cell adenoma	1	Bilat SEEG	14	6	N	None	4/mo	Bilat occipital	2	16	1/mo
4	11, M	Neonatal insult	Grade IV IVH, ADHD	3	Bilat SEEG	16	8	N	None	20/day	Lt hippocampal & lt occipital	2	16	8/day
5	17, M	Neuronal migrational abnormali-ties	Depression, congenital vascular hamartomas (s/p removal), exertion-al syncope (s/p cardiac monitor implant)	2	Lt SDG & DE ×2 Lt SEEG	92 contacts 12	7	N	SDG/corti-cectomy	12/mo	Lt hippocampal & lt parietal	2	10	0/mo
6*	18, M	Cortical dys-plasia type 2A & gliosis	Depression, OCD	3	Lt SDG Lt SEEG	64 contacts 5	7 7	N	SDG/corti-cectomy	2/wk	Lt posterior insula & lt frontoparietal	2	9	1/mo
7	17, F	CNS vasculitis	Developmental delays	3	Bilat SEEG	16	13	N	VNS	5/day	Bilat insula	2	9	8/mo
8	8, F	Unknown	None	2	Bilat SEEG	15	3	N	None	2/mo	Bilat parietal	2	7	0/mo

ADHD = attention-deficit/hyperactivity disorder; AED = antiepileptic drug; AH = amygdalohippocampectomy; ASD = atrial septal defect; DE = depth electrode; FU = follow-up; IVH = intraventricular hemorrhage; LITT = laser interstitial thermal therapy; OCD = obsessive-compulsive disorder, PRES = posterior reversible encephalopathy syndrome; pt = patient; s/p = status post; Sz = seizure; VNS = vagus nerve stimulator; VP = ventriculo-peritoneal; VSD = ventriculoseptal defect.

* Patient 6 did not have any recordable seizures after RNS implant for 8 months. He had one seizure in the 9th month, and the RNS is currently in detection mode only.

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TABLE 2. Patient cohort RNS data

Pt No.	Lead Location	Electrode Spacing	Bipolar/Cathode or Anode; Lead to Lead	Charge Density ($\mu C/cm^2$)	Pattern Detection	Average No. of Stimulations/Day
1	Rt hippocampus	DL330-10	Bipolar	4.1	Bandpass & line length	3000
2	Lt hippocampus	DL330-10	Bipolar	2.5	Bandpass & line length	2000
3	Bilat occipital	DL330-10	Bipolar	2.5	Bandpass	2500
4	Lt hippocampus & lt occipital	DL330-10	Bipolar	2.5	Bandpass	4000
5	Lt hippocampus & lt parietal	DL330-10	Lead to lead	0.5	Bandpass	400
6*	Lt frontoparietal & lt insula	DL330-10	NA	0	Bandpass	0
7	Bilat insula	DL330-10 & DL440-10	Bipolar	1	Bandpass	5000
8	Bilat parietal	DL330-10	Bipolar	1	Bandpass	1500

NA = not available.
* Patient 6 did not have any recordable seizures after RNS implant for 8 months. He had one seizure in the 9th month, and the RNS is currently in detection mode only.

the RNS device, as estimated by a nonsterile implant. Ideally, the larger incision made for the generator included at least one of the planned lead entry points to minimize the need for multiple incisions on the scalp. Care was taken to bend the arms of the ferrule to allow the generator to sit flush with the outer cortex and not produce compression on the dura mater or to put pressure on the patient's overlying skin. The generator was oriented in a way that also provided easy access for battery replacement, wherein the surgeon would only need to reopen a portion of the prior incision to replace the generator (Fig. 2). Stereotactic depth electrodes were placed prior to the craniectomy for generator insertion to ensure that accuracy was maintained with initial positioning and registration (Fig. 3). An intraopera-

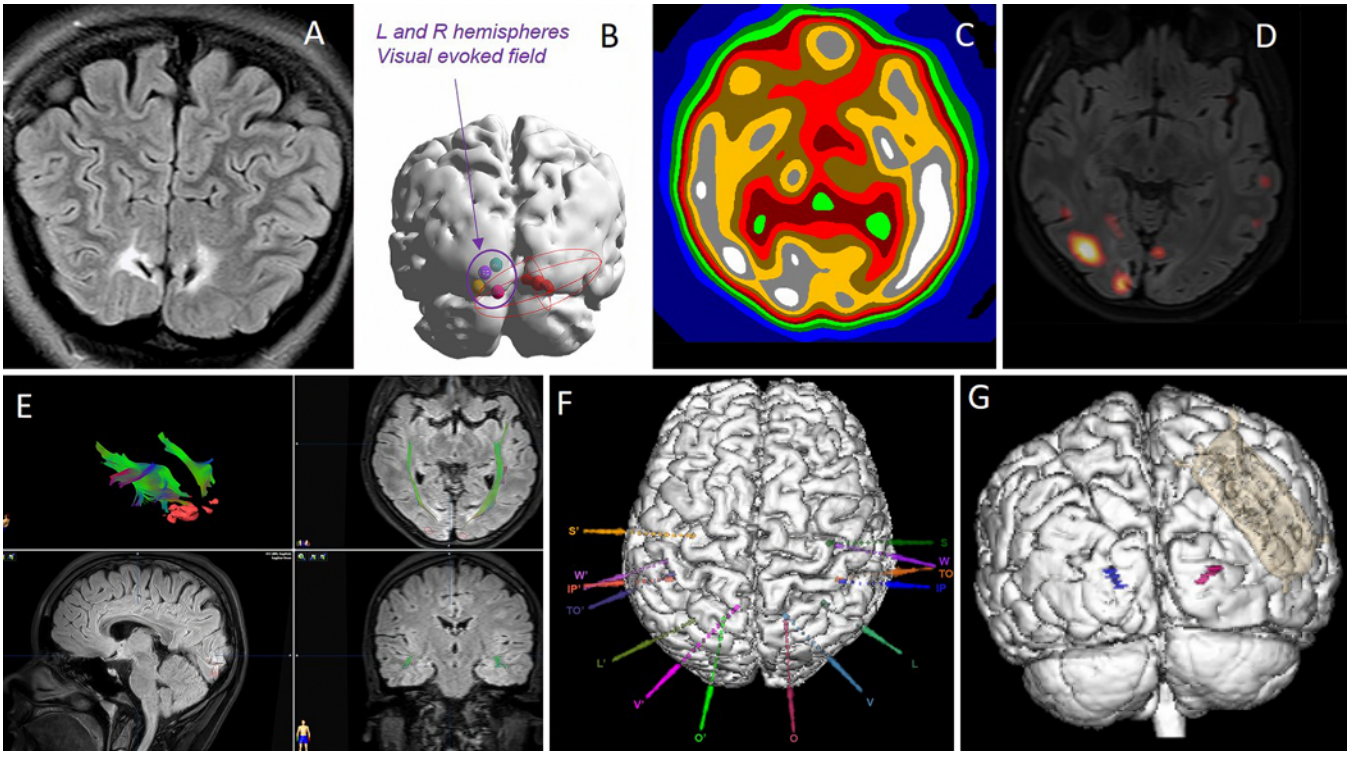

FIG. 1. Patient 3. This patient had intractable seizures after severe hypoglycemic insult secondary to hyperinsulinism from islet cell adenoma. **A:** Coronal FLAIR sequence MR image demonstrating bioccipital insults. **B:** Magnetoencephalography source localization with equivalent current dipole showing sources localizing in the right inferior occipital head region. The electrographic seizure localized at onset to the right inferior occipital lobe with subsequent spread to the left inferior occipital lobe. Right and left hemifield visual evoked fields both demonstrated localization to the left occipital lobe. **C and D:** Ictal SPECT scans. Isotope was administered 24 seconds after onset of ictal EEG changes from an electroclinical seizure originating from the right occipital region. **E:** Functional MR images of visual fields with representation of bioccipital lesions (*red*) and visual tractography (*green*). **F:** Three-dimensional CT reconstruction of bilateral SEEG. Ten seizures were recorded during monitoring, 4 with ictal onset localized to the left O' electrode and 6 localizing to the right O electrode. **G:** Three-dimensional CT reconstruction of RNS and final bioccipital lead placement. Figure is available in color online only.

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tive CT scan was obtained to ensure that no intracranial complications from the lead placement were identified. In most cases, the surgeries were performed in a hybrid operating room with 3D CT available intraoperatively.

Results

Demographics

Eight patients underwent RNS System implantation at Cincinnati Children's Hospital Medical Center between January 2019 and August 2021. All patients met clinical criteria for implantation of the RNS System after review by the multidisciplinary surgical epilepsy team at our institution. Six of 8 patients had private insurance, and their surgery was approved without additional peer-to-peer review or appeals for denials. The 2 patients without insurance had the cost of the surgery covered by the hospital as charitable cases. The average patient age at the time of RNS implantation was 14.7 years (range 8–17 years). As demonstrated in Table 1, patients had a variety of etiologies of epilepsy, including posterior reversable encephalopathy syndrome, neonatal injury, cortical dysplasia, severe hypoglycemia, CNS vasculitis, neuronal migrational abnormalities, and 1q21.1 microdeletion. In addition, 7 of the 8 patients had significant comorbidities unrelated to seizures, including intraventricular hemorrhage, hydrocephalus, congenital cardiac disease, and pancreatic tumor (Table 1). Four patients (50%) underwent a prior surgical procedure to treat medically refractory epilepsy and experienced recurrent or residual seizures. These included 1 patient with a vagus nerve stimulator, 2 patients who underwent craniotomies for seizure focus resection, and 1 patient who underwent laser interstitial thermal therapy.

Surgical Considerations

The mean surgical time for all hybrid operating room cases was 260 minutes (SD 46.1 minutes). The mean estimated surgical blood loss was 33 ml (SD 27.6 ml). No intraoperative or postoperative transfusions were required. All leads were accurately placed according to the preoperative plan and confirmed with intraoperative imaging.

Detection and Stimulation Procedures

All patients received an RNS-320Ms model. After implantation, the device was interrogated and placed into detection-only mode. Using the manufacturer's suggested protocol, a "line length" detector, which determines ictal change based on a running sum of distances between successive points of the electrocorticography time series within the sliding window of a given size, was used for initial seizure detection. As of the last visit, 6 of the 8 patients now have detection settings using bandpass filters exclusively to capitalize on the prominent low-voltage beta and gamma activities commonly present at ictal onset. Two of 8 patients have both bandpass and line length detectors enabled. Stimulation was initiated once clear seizures were recorded, typically at 1 month postoperatively, although in 2 cases this was delayed. For 1 patient, stimulation was delayed until 3 months postoperatively after seizures were recorded. For patient 6, lack of clarity about discrete seizures postimplantation has resulted in an order for a video-EEG, and stimulation was withheld for 8 months. In the 9th month, the patient had a clinical seizure and detection was enabled at that time. He is currently not undergoing stimulation. For all other patients, stimulation was started at 0.5 μC/cm^2, pulse width of 160 μsec, duration of 100 msec, and frequency of 200 Hz. Every 3 months, detection was adjusted as needed to capture the earliest ictal change, and charge density was increased by 0.5 μC/cm^2 as indicated for continued seizures, up to a maximum of 4 μC/cm^2. The stimulation field was bipolar, adjacent contact, in 5 of the 7 patients undergoing stimulation. The other 2 patients had lead-to-lead stimulation to provide a more diffuse applied electrical field. In the 7 patients undergoing stimulation, the average number of stimulations per day was 2629 (Table 2).

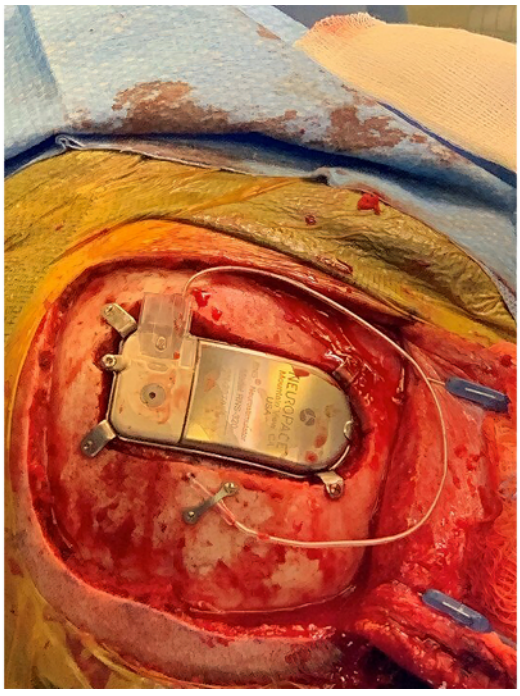

FIG. 2. Intraoperative photograph of right-sided RNS placement with the lead inserted into the hippocampus from a posterior approach. Note the placement of the RNS System within the exposure, which will allow replacement of the unit without reopening the whole incision and reduced risk to severing the lead inadvertently. Figure is available in color online only.

Surgical Complications After RNS Placement

One adverse event occurred in our series. A patient developed erythema and drainage from the cranial flap 2 weeks after surgery. Cultures were obtained from the wound, and these were positive for *Pseudomonas aeruginosa*. The patient was then taken to the operating room for complete removal of the RNS System. After a 6-week course of intravenous antibiotics was completed, the patient was brought back to the operating room for reimplantation of the RNS System. At the time of the latest follow-up, there were no further complications, and the patient benefited from a reduction in seizure frequency.

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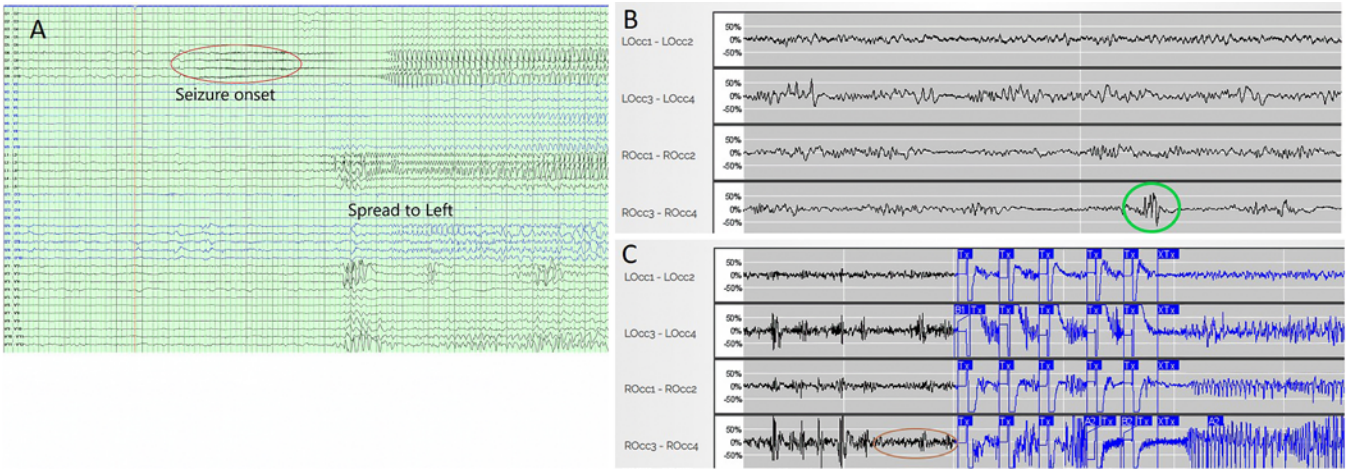

FIG. 3. A: Patient 3. Bilateral posterior quadrant stereo-electroencephalogram with selected contacts shown at ictal onset of a typical event (*red oval*). Right hemisphere electrodes are shown in the *upper half*, and left hemisphere electrodes appear in the *lower half*. Bipolar recording montage with a 1-Hz low-frequency and no high-frequency filter. At seizure onset, a band of low-voltage gamma activity was present in the right occipital pole (O6–10) contacts, followed by spread to other right occipital cortex (L electrode in Fig. 1) and left occipital spiking (O'5–9). Note the absence of fast frequency activity of ictal morphology in the left hemisphere. Rhythmic spiking best developed in ictal onset contacts O6–10. **B:** Intraoperative recording of newly implanted electrodes, with the left occipital montage in the *upper half* and the right occipital montage in the *lower half*. Lateral right occipital contact complex spike morphology is shown (*green oval*). **C:** Typical recording from the extraoperative RNS device, demonstrating ictal onset and spread consistent with previously seen seizures recorded on SEEG. Diminution of interictal discharges and development of gamma activity were seen in the lateral right occipital montage (ROcc3–4) at ictal onset (*brown oval*), followed by rapid spread to the left hemisphere and best spike development in ROcc3–4 (consistent with the O6–10 target region on SEEG). *Tx flags* indicate stimulation therapy for seizure detection. Figure is available in color online only.

Follow-Up and Seizure Outcomes

Follow-up for our group of patients ranged between 7 and 39 months with an average follow-up period of 16.5 months. All patients achieved > 50% reduction in their seizure frequency (Table 1). The mean reduction in seizure frequency was 84.4% (SD 14%).

Discussion

Managing medically refractory epilepsy in pediatric patients remains a challenge for epileptologists and epilepsy surgeons alike. This is particularly true in pediatric patients who have a difficult-to-localize seizure focus, multiple and/or bilateral foci, or eloquent localization, or in whom previous surgical therapy has failed. In our initial experience with RNS, we applied concepts previously described in the adult epilepsy surgery literature to one of the most difficult groups of patients evaluated by our comprehensive epilepsy surgery team.[7,8] Our case series demonstrates the safety and effectiveness of off-label RNS System implantation in the pediatric population, as previously reported in the literature. The RNS System was successfully implanted in all 8 pediatric patients.

Our patient population provides a broader range of seizure foci targets than previously reported in the pediatric literature.[9–13] These include not only mesial temporal structures but also bilateral frontal, parietal, occipital, and insular targets, thus expanding the potential use of RNS for various seizure foci. Targets were identified prior to RNS implantation using noninvasive and invasive monitoring with SDG and/or SEEG implantation to best characterize the epilepsy network and identify targetable seizure onset zones. Ultimately, SEEG was the modality used to identify the specific targets implanted. Our series also demonstrates the usefulness of RNS as an option for patients who underwent prior surgical interventions that were unsuccessful at effectively controlling seizures. The RNS System, therefore, can be included as part of a comprehensive treatment strategy for medically refractory epilepsy and can be performed in combination with other surgical and medical treatment strategies safely. Clinical decision-making leading to RNS implantation over other neuromodulatory brain stimulation devices (vagus nerve stimulators or deep brain stimulators) at our center involves a multidisciplinary assessment of invasive monitoring data and eloquent cortex identification. Patients with one to two well-delineated seizure networks on SEEG, for which one or both foci are in eloquent cortex, are deemed the best candidates for RNS implantation.

All 8 patients in our series experienced at least a 50% reduction in seizures from their preoperative baseline (mean 84.4%). The early positive response combined with the established literature demonstrating increasing efficacy of RNS over time are favorable factors suggesting that RNS is a useful tool in pediatric epilepsy management.[14,15] Treatment with the RNS System is primarily modulatory rather than ablative and can be modified with time and maturation of the brain. Improvements with time in response to RNS therapy have also been observed.[5,11,15,16] The effect may be due to neuroplasticity, a feature that may be particularly effective in developing brains. We expect that with further modulation and a longer temporal

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perspective, our patients may continue to demonstrate improvement in seizure outcomes.

Optimal parameters for neuromodulation are currently unknown. Therefore, for detection and stimulation settings, we have found that starting with parameters similar to those used in adult clinical trials seems successful in our pediatric population. It has become our practice to maximize beta and gamma frequency detection early while programming, to capture the "buzz" seen at ictal onset in the majority of our population. Hence, we have used bandpass filters more often than line length detectors. It is possible that bandpass filters, which detect root-mean-square amplitude, may be more sensitive for power modulations of shorter duration compared with line length detectors.[17] There are three potential mechanisms by which pediatric patients may benefit from RNS: 1) a microlesional effect resulting in disruption of tissue and disabling the epileptic network, 2) "responsive" stimulation adapting targeted stimulation to peri-ictal waveform detection, and 3) neuromodulation. The 8-month seizure freedom noted in patient 6 may be due to a microlesional effect secondary to surgical implantation. Microlesional effects have also been reported in deep brain stimulator implantation with a reduction in tremor or even after SEEG implantation with a reduction in seizures without further ablation, stimulation, or resection.[18] The microlesional effect is hypothesized to be the result of a neuroinflammatory activation of astrocytes and microglia in animal models.[19] The potential dynamic of these three mechanisms should be an active area of study in future.

Our early experience indicates that pediatric RNS has a dynamic effect on the individual patient. As a guideline, we recommend that all patients undergo pre- and postsurgical neuropsychological examination. These data will be included in a larger analysis, as follow-up is currently ongoing. We hypothesize that working memory and processing speed may improve with improved seizure control, although potential negative effects of neurostimulation in different brain regions have not been sufficiently explored.

We experienced one complication of a deep wound infection requiring return to the operating room for explant of the RNS System. After the system was explanted and the patient was treated with an appropriate course of intravenous antibiotics, the RNS System was successfully reimplanted using the patient's previously achieved detection and stimulation settings. We used the same craniectomy site for the reimplantation. The infection did not recur, and the implant was able to be used successfully with a reduction in the patient's seizures. Despite targeting eloquent areas, no adverse RNS events occurred in our patient cohort. As a small retrospective review, this work is not without limitations. Results may have been affected by patient selection bias and relatively short follow-up as well as partially relying on patient diaries for determination of seizure outcomes.

Conclusions

Our small retrospective pediatric series of carefully selected patients highlights recent advances specifically in SEEG and RNS technology that have advanced the field of pediatric epilepsy surgery. Patients, who not long ago may not have been considered surgical candidates, are now enjoying significant reductions in disabling seizures.

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Disclosures

Dr. Tenney: consultant for Persyst. Dr. Air: consultant for Stryker and Functional Neuromodulation; and clinical or research support for the study described from Medtronic.

Author Contributions

Conception and design: Mangano, Greiner. Acquisition of data: Mangano, Hartnett, Leach. Analysis and interpretation of data: Mangano, Hartnett, Greiner, Arya, Tenney, Aungaroon, Holland, Air, Skoch. Drafting the article: Hartnett. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Mangano. Statistical analysis: Hartnett. Study supervision: Mangano.

Supplemental Information

Previous Presentations

A portion of the data included in this article was presented at the AANS/CNS Section on Pediatric Neurological Surgery meeting as an e-poster, Salt Lake City, Utah, December 7–10, 2021.

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