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Mini Review

Responsive Neurostimulator Clinic: Lessons Learned and Advocacy for a Multidisciplinary Approach

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Abstract

We have been running a multidisciplinary RNS clinic since 2021 and advocate for such an approach. Our team has been able to achieve better than published results with RNS. Our team consists of Neurologists, a Neurosurgeon, a coordinating nurse practitioner, a neuropsychologist, a social worker, and the RNS representative. Our clinics involves data review, deliberation, patient evaluation, planning for changes to RNS settings, and follow-up. We have identified certain principles to RNS care. Namely, these are the requirement of patient engagement, early acknowledgement that network modulation takes time, and that once placed and RNS cannot be seen as having failed until 3 years of active engagement have been achieved. We believe that all centers providing RNS therapy should employ a structured multidisciplinary approach to achieve the best outcomes in the shortest time.

INTRODUCTION

Epilepsy affects 1-2% of the general population with 35% of these patients developing drug resistant epilepsy (DRE). Epilepsy surgery can yield a seizure freedom rate of around 64.8% in cases of DRE [1]. Responsive neurostimulation (RNS) has emerged as a promising therapy allowing patients otherwise contraindicated to resective epilepsy surgery to benefit from a surgical treatment. The power of this treatment modality has expanded surgical indications to include multi-focal and even generalized epilepsy [2]. The device involves implantation of one or two electrodes with four contacts each in or near a seizure focus or network hub and connection to a generator implanted into the skull. It is a closed system that can detect intracranial electrocorticographic (iEEG) signals as well as provide stimulation. Understanding of the exact mechanism of RNS is evolving, with most recent perspectives focusing on the system's network modulating power [3]. Patients with complex and special needs have been shown to benefit from multidisciplinary clinics in multiple domains [4-7]. We advocate for a multidisciplinary approach to RNS and share our experience running a multidisciplinary RNS clinic.

LESSONS LEARNED

We have been running a multidisciplinary RNS clinic since 2021. The clinic occurs once per month and is made up of a lead epileptologist, the neurologists following individual RNS patients long-term, a neurological surgeon, a neurology team nurse practitioner, a social worker, and the RNS representative. A typical clinic involves a team huddle with review of the patient's history, review RNS iEEG data over time, recommendation of changes to detection or stimulation settings from the RNS representative, discussion with potential modification of proposed changes, evaluation of the patient with presentation of plan to patient and family, implementation of plan with ongoing follow-up. We have learned lessons that we believe should influence standard practice in RNS care.

Complex needs in patients with limited resources

The needs of RNS patients are imposing. These patients have DRE at baseline and come with all of the common associated struggles. They have had a device implanted into their head utilizing a complex method to deliver care to a complex disease. These patients and their families must be active participants in their care to achieve optimal success as the team cannot learn from and modify the device settings with efficacy without data actively uploaded by the patient regularly. Economic resources of epilepsy surgery patients have been shown to influence care delivery [1]. Our patient population is uniquely challenged, although with excellent support from state resources. Our team's social worker has been instrumental in maintaining the connectedness of our RNS patients, providing a lifeline enabling their participation in RNS care. One of our early RNS cases

developed a psychiatric disorder making travel to clinic difficult. We have been able to virtually integrate this patient into RNS clinic by team discussion of uploaded data from family and the patient's Neurologist making as needed home visits for any necessary changes to settings.

Surgical Questions

All patients in RNS clinic have had surgery involving the implantation of a medical device into their head. There are inevitable questions of a surgical nature that routinely arise; eg, 'this certain part of my wound throbs from time to time, why is that?', 'what is this bump on my head?', 'what is generator replacement going to be like?', etc. The presence of the team's primary epilepsy surgeon is instrumental in transforming these questions into passing concerns. Having a broad range of expertise on the team enhances trust by creating a team environment readily responsive to the patient's concerns as they arise. This is critical as the success of RNS requires active patient participation over time.

The Complex Marathon of Network Modulation

RNS is now seen primarily as a network modulating modality [3], a process that does not happen overnight. We have learned to trust the well published phenomenon of improved RNS outcomes over time [8], but this requires active learning and engagement of all parties. We explain to all RNS candidates that they must anticipate a learning curve that may take months to years to achieve their desired outcome. We implanted a bilateral hippocampal RNS into a patient with pre-operative data demonstrating temporal seizure activity occurring more frequently on the left than the right. About 10 months after RNS implantation, we had found only right sided seizures on RNS iEEG and stimulation in response brought no benefit, frustrating the family. We deliberated this, performed scalp EEG with RNS in place, and even considered removing the RNS device for redo invasive pre-operative studies. However, after careful review of the literature and team discussion, the decision was made to turn on stimulation on the left side even though we were not detecting seizures. Now, about 1.5 years after implantation, we have achieved the elimination of all long epileptiform episodes on iEEG as detected by RNS and the patient has experienced dramatic clinical improvement.

OUTCOMES

Since February 2020, our team has placed a total of 12 RNS devices. Of these, 10 have at least one follow-up since turning stimulation on, if indicated. Of these patients with follow-up, 80% of cases have a 70% or better improvement in seizures, representing responders. Super-responders with 90% or greater improvement represent 40% of the cohort. Only two (20%) patients in our cohort have been non-responders with <50% improvement. With less than 5 years of follow-up in all cases and when measured conservatively based on evaluation in clinic, our median percent reduction in seizure frequency and severity is at least 75%. The RNS Pivotal trial based on 2 years of follow-up demonstrated median percent reduction in seizures of 53% in adults [9]. A follow-up study to this with 9 years of follow-up reported a median percent seizure reduction of 75%, a responder rate of 73%, and a super-responder rate of 35% also in adults [10]. The more limited pediatric literature demonstrates that at 12 months follow-up a median percent seizure reduction of 75% in a cohort with 18% super-responders can be expected [11]. Therefore, our overall seizure reduction is on track with RNS trends in the literature but we are achieving an enhanced rate of super-responders on a compressed timescale.

Advocacy for Multidisciplinary Approach to RNS clinic

We believe that our multidisciplinary approach to the care of RNS patients with a dedicated RNS clinic has enabled us to achieve better than published outcomes with our RNS patients. Our RNS clinic is part of a broader epilepsy surgery multidisciplinary conference schedule well attended in our level 4 epilepsy center. We have developed certain policies that we maintain with our patients and team. First, RNS requires active engagement with long-term learning. The patient is part of the team and their engagement supplies the data. Second, network modulation takes time. We do have lucky patients with very early response to therapy, however it is more common that tweaks need to be made iteratively over time. We have established that an RNS system has not 'failed' until it has been utilized and activity engaged for at least 3 years with no improvement or with worsening of seizures. It is important to not give up on RNS therapy prematurely once implanted. We believe that these tactics can and should be employed by all teams providing RNS therapy to achieve maximized benefit.

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