



## Vagus nerve stimulation and magnet use: Optimizing benefits

William O. Tatum IV<sup>a,b,\*</sup>, Sandra L. Helmers<sup>c</sup>

<sup>a</sup> Tampa General Hospital, Tampa, FL, USA

<sup>b</sup> Department of Neurology, University of South Florida, Tampa, FL, USA

<sup>c</sup> Emory University of Medicine, Atlanta, GA, USA

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### ABSTRACT

More than 10 years ago, the vagus nerve stimulator became the first device approved by the Food and Drug Administration for use in persons with epilepsy. The vagus nerve stimulator has subsequently served to spearhead the concept of neurostimulation for seizures. Chronic intermittent electrical stimulation of the left vagus nerve is the foundation for vagus nerve stimulation, yet little is known about its capability to deliver acute, on-demand, activation of stimulation through use of a magnet. Thus far, clinical use of magnet-induced vagus nerve stimulation has not been elucidated. In an effort to help guide management, we highlight current and potential uses of acute abortive therapy with vagus nerve stimulation. We review the current evidence that is available for vagus nerve stimulator magnet use, discuss potential clinical applications that exist, offer a protocol for magnet application within the institutional setting, provide our approach to titrating the magnet parameters, and make recommendations for magnet use that support an evolving standard of care.

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### 1. Introduction

Although more than 49,000 patients with medically refractory epilepsy have been implanted with a vagus nerve stimulator (VNS) [[AU: To avoid confusion the abbreviation VNS has been reserved for “vagus nerve stimulator”; “vagus nerve stimulation” is written out, not abbreviated.]] over the decade since it became available [1], there is relatively little information on the role of magnet-induced stimulation in the management of recurrent seizures. The magnet mode is a unique feature of the VNS that enables the patient or caregiver to provide immediate on-demand stimulation by passing the magnet over the pulse generator. The magnet-activated stimulation is in addition to the regular, intermittent, electrical stimulation delivered to the vagus nerve with the normal mode. Clinicians may program the pulse generator to deliver stimulation at different settings as desired for the normal and magnet modes. Some patients and caregivers who have used the magnet to activate stimulation during an aura or at the onset of seizures have reported aborting the seizure, lessening its severity, or decreasing the postictal period. In addition to activating on-demand stimulation, the magnet can be held in place to stop stimulation temporarily. Although many clinicians are aware of the aspects of managing seizures and temporarily stopping stimulation with the magnet, other uses for the magnet and their implications

have not been fully explored. We review the current literature describing magnet use to provide some background information, and share our clinical experience with other physicians using vagus nerve stimulation to promote optimal benefit for patients with epilepsy implanted with VNSs.

### 2. Initial experience with VNSs

The original work on VNSs was done by Zabara [2] in dogs and was based on acute interruption of seizures by stimulation of the left vagus nerve, giving rise to the concept of on-demand mode vagus nerve stimulation. As a result, two methods of vagus nerve stimulation were developed: automatic stimulation at preprogrammed intervals and on-demand mode stimulation initiated with a magnet. During the first randomized controlled clinical trial of vagus nerve stimulation for epilepsy (E03) in humans, patients were randomized to a treatment group with higher stimulation, whose pulse generators were programmed to deliver on-demand stimulation when the magnet was swiped over the implanted pulse generator. This group was more likely to report a benefit from magnet application than patients in the active control group with lower stimulation, whose pulse generators were not programmed to deliver magnet-activated stimulation ( $P = 0.0479$ , Fisher's test) [3]. Of 86 patients using the magnet in an open-label, compassionate-use trial (E04), 22% reported seizure termination and 31% reported seizure diminution [3]. Therefore, approximately one-half of patients who used the magnet in this study received some benefit unrelated to seizure reduction with programmed

\* Corresponding author. Address: c/o 13801 Bruce B. Downs Boulevard, No. 401, Tampa, FL 33613, USA. Fax: +1 813 971 6951.

E-mail address: [WOTIV@aol.com](mailto:WOTIV@aol.com) (W.O. Tatum).

stimulation. In the E04 trial, results of magnet use were documented for 9482 seizures, of which 2211 (24%) resulted in seizure termination, 3638 (38%) resulted in seizure diminution, and 3633 (38%) had no effect. In both the E03 and E04 trials, the magnet mode output current was the same as normal mode, which ranged from 0.25 to 3.0 mA in E03 and from 0.25 to 3.5 mA in E04. Magnet ON time ranged from 30 to 90 seconds in E03, and was 30 seconds in E04. Pulse width was 500  $\mu$ s in both trials [3].

Postmarketing experience with the magnet has been recorded in a sponsor-held VNS patient outcome registry. In late 1998, the manufacturer developed patient registration of VNS use that compiles and maintains information obtained from multiple sources. Patient demography, medical history, number and frequency of seizures, device settings, efficacy, adverse events, and quality of life with information were collected at stimulation initiation and at 3, 6, 12, 18, and 24 months afterward. Of the 2696 patients implanted with stimulators enrolled in the registry and with data at 12 months after implantation, 1665 (61.8%) reported magnet use, and 1418 (85.2%) of those self-reported at least some positive effect of the magnet on their seizures. For 1001 (60.1%) patients, someone other than the patient applied the magnet [1].

Magnet use may also impose the potential for adversely affecting other objects and medical devices. The field strength of the magnet is at least 50 G at 1 inch and may damage electronic media such as credit cards, computers, and similar objects in addition to activating the generator if it is carried too close to the chest. With respect to cardiac pacemakers or defibrillators, thus far we are not aware of any instances of magnet use adversely affecting their function. However, magnet interaction with programmable shunt valves has been reported. An *ex vivo* trial conducted by Jandial et al. [4] demonstrated that the external magnetic fields generated by the magnet could affect programmable shunt valves. With the magnet 4 cm from the Strata programmable shunt valves (Medtronic Neurosurgery, Goleta, CA, USA), the magnetic field changed the pressure setting of the valves in 78 of 100 trials. A single case reported by Guilfoyle et al. [5] described a stimulator-implanted patient wearing a magnet on her wrist who unexpectedly affected a Strata shunt and caused insufficient diversion of cerebrospinal fluid probably by repeatedly adjusting her ponytail.

In the initial experience with VNSs, both benefits and risks regarding the magnet use have been described in patients with epilepsy. The foundation of knowledge of magnet use from the clinical trials and postmarketing experience has led the way to recommendations for use where clinical experience has been limited.

### 3. VNS magnet: Current recommendations for clinical use

The VNS pulse generator operates in two modes: the normal mode, which delivers the regular, intermittent stimulation to the

vagus nerve, and the magnet mode, which enables the patient or a caregiver to activate immediate, on-demand stimulation [2]. Table 1 compares the VNS normal mode with the VNS magnet mode and lists the uses and purposes of both.

#### 3.1. Titrating the magnet mode

Although algorithms for titrating VNS normal mode parameters have been published [3,6], a detailed approach to titrating the magnet mode has not been available previously. The following suggestions focus on maximizing the benefits of the VNS magnet mode.

The magnet mode output current and magnet mode ON time must be titrated to an individualized *effective abortive threshold*, the combination of magnet mode parameters that enable the patient or caregiver to prevent or stop a seizure by swiping the magnet. Initiate the magnet mode output current at 0.25 mA higher than the normal mode output current. Options for magnet mode ON times are 7, 14, 21, 30, and 60 seconds. Select either 30 or 60 seconds, depending on the patient's tolerance. Select pulse width and signal frequency to reflect the settings used in the normal mode parameters. An OFF time is not used in the magnet mode. The magnet mode parameters may be assessed during routine device interrogation and programming. The stimulation should be tolerable for the patient, and its effectiveness at aborting or diminishing seizures may be assessed through patient or caregiver report.

Once the effective abortive threshold has been achieved, the magnet mode parameters should be held constant even when the output current and duty cycle for the normal mode may change or increase. For some patients, the magnet-activated output current may be less than the normal mode output current when the magnet has been effective at a lower output current setting. When an effective abortive threshold has not been achieved, the magnet mode output current should be titrated with the normal mode parameter settings. The magnet mode output current setting should be set 0.25 mA higher than normal mode settings and increased until an effective abortive threshold is achieved (Table 2).

#### 3.2. Magnet applications

Many patients with temporal lobe epilepsy experience an aura before the onset of a seizure [7], or a family member or caregiver may recognize seizures during the initial stages. Both of these circumstances offer the opportunity to activate stimulation with the magnet at the onset of the seizure. In our clinical experience, delivery of magnet-initiated stimulation may abort, shorten, or even

**Table 1**  
Comparison of VNS normal mode with VNS magnet mode.

|                | Normal mode                                   | Magnet mode  |
|----------------|---|--|
| Stimulation    | Programmed, regular, intermittent stimulation | Immediate, on-demand stimulation   |
| Implementation | Automatic cycling that is parameter specific  | Swipe the magnet over the generator to deliver acute preprogrammed stimulation   |
| Purpose        | Reduce seizure frequency                      | 1. Acutely stop a seizure with magnet activation<br>2. Stop stimulation by keeping the magnet in place over the generator<br>3. Check generator battery function |

**Table 2**  
Magnet mode titration to an individualized effective abortive threshold.

| Magnet mode parameter | Adjustment   |
|-----------------------|--|
| Output current        | Initiate at 0.25 mA above the normal mode output current<br>Increase (usually in 0.25-mA increments) as required                                 |
| ON time               | 30 or 60 seconds, depending on patient tolerance (60 seconds is the maximum duration permitted by the device's software)<br>Increase as required |
| Pulse width           | Initiate same as normal mode   |
| Signal frequency      | Initiate same as normal mode   |
| OFF time              | Not used in magnet mode  |
| Magnet swipes         | Swipe the magnet successively for a total of three times at 1-minute intervals if the seizure does not cease                                     |

*Note.* Clinicians often begin titration of the magnet mode by setting the ON time at 60 seconds and increasing the output current to achieve an effective abortive threshold [5]. If tolerance of the magnet-induced stimulation becomes an issue, the ON time can be reduced to 30 seconds.

terminate acute repetitive seizures or focal status epilepticus. Another use of the magnet is to control side effects associated with vagus nerve stimulation. For example, if a patient experiences pain or discomfort at the site of stimulation during normal mode stimulation, securing the magnet over the chest wall at the site of the pulse generator with tape or other means will terminate stimulation until interrogation and diagnostics or reprogramming can be performed nonemergently. Similarly, patients with voice quality that is adversely affected by stimulation may temporarily stop stimulation by securing the magnet over the generator during the time they participate in activities such as public speaking and singing, to avoid any hoarseness that may occur during stimulation. A third use of the magnet is to check that the generator is functioning. The manufacturer recommends a daily swipe of the magnet to activate the magnet mode. Because some patients become accustomed to the intermittent stimulation they receive in the normal mode, output current in the magnet mode is usually set higher than the normal mode, to allow detection of the generator function. For patients who are reliably able to detect the intermittent stimulation, daily checks are superfluous and unnecessarily deplete battery capacity.

Patients who function independently can perform magnet functions related to aborting seizures, stopping stimulation, and testing the battery. For patients who are dependent on a caregiver, particularly in schools and the institutional setting, someone other than the patient will be required to apply the magnet. The clinician should ensure that clear instructions are in place to direct the staff on the proper use of magnet-induced stimulation. Acute abortive protocols are designed to allow magnet-induced stimulation and should be based on the magnet mode time to cycle (duration), which is usually up to 60 seconds. For example: For acute repetitive seizures, prolonged seizures, and status epilepticus, the caregiver should attempt to abort the seizure by swiping the magnet successively three times at 1-minute intervals (see Table 3 for more details). Distinguishing between prolonged seizures and status epilepticus may be more academic than pragmatic, as the sooner treatment is delivered, the greater the likelihood of response [8,9]. The manufacturer's information about magnet application does not set a specific limit on the number of successive activations with the magnet; it does, however, caution against continuous swiping of the magnet for more than 8 hours [3].

**Table 3**

Directives for nursing staff who care for VNS-implanted patients in an institutional setting.

*Suggested protocol*

1. At the earliest sign of an aura or during a breakthrough seizure, magnet activation should be initiated on a "PRN" basis and according to standard use.
2. Initiate magnet activation immediately for
  - seizures exceeding 5 minutes
  - acute repetitive seizures (i.e., two or more seizures separated by less than 15 min).
3. Attempt to activate VNS with the magnet in accordance with physician directives.
  - Swipe the magnet successively three times at 1-minute intervals.
4. Use magnet activation in parallel with optimized medical management.
5. If the seizure does not stop within 5 to 10 minutes, initiate patient transport to the hospital, depending on individualized physician-directed specifications.

*Example of written orders*

1. For acute repetitive seizures, defined as more than two seizures occurring in less than 1 hour or prolonged seizures of more than 5 minutes' duration, swipe the magnet over the area where the generator is implanted every 1 minute  $\times$  3 or until seizure termination.
2. Physician notification and other abortive therapies (e.g., oral or rectal benzodiazepines) should be instituted at the direction of the prescribing physician.
3. Transportation for acute emergency care in the event that acute abortive treatment fails should be individualized and initiated at the direction of the prescribing physician.

## 4. Future directions

The magnet mode settings have traditionally been based on the maintenance mode settings. Although the uses below reflect potential applications of on-demand acute vagus nerve stimulation, further studies are needed to determine the situations that might be useful for clinical seizure control or reduction. The optimal magnet mode settings, particularly in those patients who do not clearly respond to on-demand stimulation, will more fully be elucidated with controlled prospective parameter trials that include magnet adjustment.

### 4.1. Prophylactic use of the magnet

Some anecdotal reports from the author's patients pertain to the prophylactic use of the magnet for circadian seizures. Patients whose seizures occur in patterns have reported preventing the seizures by applying the magnet before their anticipated occurrence. For example, patients who have experienced morning seizures have reported fewer occurrences, seizures of shorter duration, or a shorter postictal period after they have applied the magnet on awakening. A trial investigating the outcome of prophylactic magnet use would entail review of seizure diaries to establish the pattern of circadian seizures, documentation of prophylactic magnet use, and follow-up review of seizure diaries.

### 4.2. Reductions in use of rescue medications and medical utilization

A reduction in the use of antiepileptic drugs (AEDs) has previously been reported following implantation of a VNS when compared with a control group [10]. Similarly, patients and caregivers who are able to activate the magnet mode stimulation and thereby abort or lessen the severity of a seizure may report a reduction in the use of rescue medications and sometimes a milder and shortened postictal period. For example, patients who have experienced prolonged somnolence during the postictal state after a seizure may be able to recover more quickly and resume their normal activities earlier than expected following use of the VNS. A controlled trial to document a change in the use of rescue medications before and after implantation with a VNS, when compared with the degree of success with magnet use, could substantiate or refute these anecdotal reports. In addition, reported changes in emergency department (ED) visitation and seizure-related hospitalizations could be evaluated.

### 4.3. Magnet use in the residential setting

In developmentally disabled patients with mild to severe mental retardation and refractory epilepsy, Andriola and Vitale [11] performed a retrospective chart review and reported that 11 of 16 (68%) clearly evaluable patients aged 3 to 56 years had a greater than 50% seizure reduction at 6 months. Family caregivers and institutional staff were provided pre- and postoperative education on magnet use and were able to apply the magnet and successfully abort or terminate seizures for many of the patients. Clinicians who follow VNS-implanted patients receiving care in an institutional setting should ensure that protocols for magnet use are in place because these patients are seldom able to activate the magnet mode without nursing assistance, as illustrated in the following vignette:

A 38-year-old male resident of a developmental center had medically refractory epilepsy following a prior craniotomy for aneurysm repair after a large right hemispheric hemorrhage. Seizures manifested as weekly, brief, "mild," acute repetitive partial seizures and status epilepticus requiring frequent rectal diazepam

and ED visitation. He was not a resective surgical candidate, and was implanted with the VNS. Afterward, he experienced a 50% overall seizure reduction and a 75% reduction in acute repetitive seizures and concomitant rescue medications as a result of acute magnet-activated vagus nerve stimulation (W.O.T., personal observation).

Table 3 provides an example of a nursing protocol for magnet activation as well as written orders for nursing personnel caring for VNS-implanted patients in the institutional setting or settings that require caretaker oversight.

## 5. Comment

Thus far, magnet-induced acute vagus nerve stimulation has received limited attention in clinical reports. Boon et al. [12] found vagus nerve stimulation to be efficacious with a favorable cost/benefit ratio in patients with refractory partial-onset seizures. The efficacy results of magnet use by 21 patients were reported. (Application of magnet function was performed by caregivers of 13 of the patients). One-third reported no effect, and the remaining patients reported some degree of effectiveness. In a report of the first 100 VNS-implanted patients in a pediatric epilepsy center, Murphy et al. [13] described patients with severely intractable epilepsy who were identified by means of operating room records during surgical implantation. Seizure reduction was independent of age and duration of epilepsy, and there were fewer adverse events in those under 12 years of age. The results of 70 patients with magnet data included 34 (49%) patients who benefited either from termination or limitation of the seizure or from elimination of the lethargy following a seizure. Thirty-five (50%) patients did not report any significant benefit, and one reported that using the magnet worsened seizures.

A proposed classification system for objective quantification of VNS outcomes lists four classes for grading changes in seizure frequency [14]. A separate category (Class IV) denotes that the VNS normal mode did not reduce seizure frequency, but that magnet use prevented seizure progression or limited seizure duration or severity. In a case series of 48 patients, 8 patients (16.5%) had Class I outcomes (80–100% reduction in seizure frequency), and 3 patients (6%) had Class IV outcomes [14]. Major and Thiele [15] used this classification system to report outcomes of vagus nerve stimulation. Of the 16 patients in their retrospective study, 8 patients (50%) were able to abort seizures with intermittent magnet use, and 1 patient had a Class IV outcome.

Success with the VNS has highlighted the use of the magnet for acute abortive therapy as an adjunct to chronic intermittent stimulation, yet there is a common misperception that the VNS can be used effectively only by patients who experience and can respond to a seizure aura. Patients frequently question whether vagus nerve stimulation is an appropriate therapy for them because they “do not have a warning” to activate their device. This misperception evolved from accounts of aborting seizures by magnet application during the early years of use for patients with auras prior to complex partial seizures. Even when patients do not experience auras, the potential importance of the patient or caregiver activating the magnet mode at the beginning of a seizure cannot be overemphasized.

In conclusion, appropriate use of the magnet virtually has no disadvantage relative to safety or overdosing. External application of the magnet by the patient or caregiver can potentially interrupt a seizure, lessen its severity, and diminish the postictal period without incurring the systemic and idiosyncratic risks inherent with traditional rescue medications. The acute abortive effects of

vagus nerve stimulation may ultimately extend to include those with acute repetitive seizures or prolonged seizures in addition to benefits realized from AED reduction. In addition, the patient may benefit from prophylactic magnet use to mitigate anticipated seizures that have occurred in a predictable pattern. Further prospective studies in patients admitted to the hospital for video/EEG monitoring could provide the grounds for controlled trials of acute VNS therapy. Nevertheless, magnet-induced vagus nerve stimulation continues to be an inherent, readily available, and a predictably safe means of pursuing immediate attempts at acute seizure termination. Thus far, although device parameters have not been shown to be the primary determinant of improved efficacy with time [16], correlating magnet use with various normal mode parameter settings might provide additional efficacy information. While expert opinion is not a substitute for evidence-based results, these observations may help provide support for use of the VNS magnet as an additional and still evolving standard of clinical care as well as for future directions in research.

## Contributors

The authors developed the basic draft of the article and oversaw all revisions. Susan E. Siefert, ELS, CBC, Principal, Medical Writing, and stockholder at Cyberonics, Inc., provided editorial services.

## Conflict of interest statement

Dr. Tatum has received honoraria/travel compensation for lectures and presentations from Cyberonics. Dr. Helmers has received honoraria for being a consultant and advisor for Cyberonics.

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