VAGUS NERVE STIMULATOR (VNS) PROGRAMMING GUIDELINES

Produced by Nurses representing Adult and Paediatric Services throughout the UK & Ireland

March 2016
(Review date March 2018)
VAGUS NERVE STIMULATOR (VNS) PROGRAMMING GUIDELINES

These guidelines were originally developed by a panel of epilepsy specialist nurses led by Cathy Queally at a series of meetings supported by LivaNova (formerly Cyberonics).

The panel would like to thank all the colleagues at LivaNova involved in the development of these guidelines for supporting the meetings and for helping to clarify numerous technical issues along the way.

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INTRODUCTION

Vagus Nerve Stimulation (VNS) is a well established treatment for epilepsy. It is indicated for use as an adjunctive therapy to reduce the frequency of seizures in children, young people and adults who are refractory to antiepileptic medication but who are not suitable for epilepsy surgery. This includes patients whose epileptic disorder is dominated by focal seizures (with or without secondary generalisation) or generalised seizures. [NICE, 2016].

Over recent years, the number of patients implanted with VNS therapy systems has increased and there has been a corresponding need for more VNS clinics to support them. These clinics are usually managed by registered nurses specialising in epilepsy who have developed expertise in programming VNS pulse generators to deliver optimal outcomes.

These VNS programming guidelines aim to capture this expertise to ensure the highest standards of care are provided to patients across the UK and Ireland. The treatment objective is always to find a regime that is safe and comfortable to the patient which maximises quality of life and seizure control.

These guidelines are intended to showcase the best practice in VNS care and to assist nurses in VNS clinics to provide a quality service to both adults and children with refractory epilepsy. Treatment pathways should be adapted to individual needs within these guidelines. Whilst these guidelines cover many aspects of VNS care, additional support can be obtained from LivaNova regional representatives (see Appendix 1.)

For programmers of VNS it is recommended that the minimum caseload of patients undergoing VNS treatment is 15, however we appreciate that this is not always geographically possible therefore in those areas with fewer patients it is recommended that these practitioners have a VNS mentor with more experience in order to support clinical practice.
Section 1: PRE-IMPLANTATION CONSIDERATIONS

All patients/family/carers considering VNS as a treatment for their epilepsy should be supplied with the information to make an informed choice. Information may be provided via leaflets, DVDs, consultation with the physician, epilepsy nurse and surgeon.

The following aspects should be covered:

- What is VNS therapy?
- How the VNS system is implanted
- Associated risk of surgery
- How the VNS generator is programmed
- Type of generator (standard or Autostim)
- Duty cycles/Autostim
- Increased outpatient appointments during the ramping up phase
- Adverse effects and how these could be managed
- Expectations of VNS Therapy
- Magnet use
- Potential improvement in quality of life
- MRI compatibility
- Replacement of generator
- Potential lead fracture

It is important to manage the expectation of the patient/family/carers with respect to commitment to attend regular clinic appointments and also the expected response of VNS Therapy within a realistic time frame. It may take up to 18 months at therapeutic range to maximize VNS therapy. The discussion should cover the following topics:

A baseline of seizure type, severity, frequency and post ictal recovery should be recorded for each patient prior to VNS implantation. It is also useful to document regular antiepileptic medication(s), rescue medication and frequency of administration and to consider measurement of quality of life using standardized measures.

When VNS surgery is planned, it is important to liaise with the theatre staff to ensure all necessary equipment is available for use by the implanting surgeon.

This equipment includes the following:

- VNS generator (models 102 Pulse, 102R Pulse Duo, 103 Demipulse, 104 Demipulse Duo, 105 Aspire, 106 AspireSR)
- VNS lead (303 Dura, 304 Flex). Both available in 2mm or 3mm diameter
- Tunneller
- Accessory Pack
- Patient Essentials Kit (magnet)
- Programming wand
- Programming Tablet
- Spare white connector cable (RS232 cable between wand and tablet)

It is advisable to have a spare of each of the above.

The expiry date and outer packaging of all equipment should be checked. To ensure sterility a gold/green spot should be evident on the sterile packaging. The programming computer will need to be adequately charged to ensure that it functions during the surgery.

If any of the above items are not available, it can take several days to arrange delivery from LivaNova Head Office in Italy.
Section 2: Intra-Operative Procedure

Equipment check list:-
- Generator, single/dual pin.
- Lead 2.0mm or 3.0mm Dura (303) or flex (304)
- Tunneller
- Accessory pack
- Programming wand (spare 9v battery)
- Fully charged programming tablet
- Patients essentials kit (magnets)
- Sterile laser arm bag

It is advisable to have a spare of each of the above.

The VNS generator should be programmed with the patient data and date of surgery immediately prior to or shortly after implantation

Step 1: Interrogating the device

- Connect the programming wand to the programming computer & switch the computer on.
- Hold the programming wand over the generator.
- From the Main Menu, select “Interrogate Device” (Interrogation is always the first and last step in a programming sequence)
• With the wand placed over the generator, select "**Start Interrogation**"

![Interrogating Device](image)

It can take up to 15 seconds for the interrogation to be completed and for the VNS pulse generated settings to be displayed.

Interrogate the generator in the sterile package.

Check that the serial number displayed on the programming screen after interrogation of the generator corresponds to that on the package.
Step 2: Program Patient Data and Implant Date

Check that the Patient ID and the date of surgical implantation have been entered and are correct. If not, program as necessary. For AspireSR this is automatically prompted for on every first interrogation unless already complete. If you wish to amend at any time then access this through the option ‘Program Patient Data’

Step 3 Intra-operative Diagnostics.

It is recommended by Livanova that a System Diagnostic Test is performed in sterile conditions when the generator is first connected to the lead and also when the full system is in situ. (The wand needs to be placed in a sterile sleeve/laser arm bag). This ensures the system is functioning correctly before wound closure. A subsequent test should also be performed following wound closure to ensure the lead has not been damaged during closure of the wound.

Step 4 Heart Beat Sensitivity Calibration (AspireSR only)

See Heart Beat Sensitivity Section 10.3
**Troubleshooting intra-operatively**

In the unlikely event that the impedance is HIGH:
- Verify that the lead is placed around the Vagal nerve appropriately
- Verify the lead is fully inserted into the generator.
- Repeat the system diagnostics

If the impedance is still HIGH
- Unplug the lead connector (s), then reconnect to the generator and repeat the system diagnostics.
- Irrigate the nerve with distilled water

If HIGH impedance continues contact your LivaNova regional representative or LivaNova helpline 0800 0461355

**Post-Operative care**

Please refer to your local policy/guidelines for choice of wound dressing and post-operative wound care.

Post-operative wound assessment and potential removal of dressing maybe performed at a separate appointment prior to activation.
Section 3: DEVICE ACTIVATION & PROGRAMMING

Initial appointment following Implantation Surgery

LivaNova recommend that the VNS be switched on two weeks after surgery (Ref Physicians Manual) however, a number of centres switch on in theatre, this should be carried out in line with local guidelines. It is important to ensure that there is no surgical wound infection present at both sites before the device is activated. If there is evidence of wound infection, liaise with the implanting surgeon to consider appropriate management of this.

Discuss scar management with the patient including the use non-perfumed moisturisers over the scars when fully healed and the use of sun protection when necessary.

Activation of the VNS Generator

The following steps should be taken to switch on the VNS generator and thereby initiate VNS therapy. (The following applies to generator models 103, 104, 105, 106).

Diagnostic testing for models 101, 102, 102R differs slightly which is explained under section 6.

The programming equipment should always be cleaned between patients with alcohol / disinfectant wipes.

Step 1: Interrogating the device

- Connect the programming wand to the programming computer & switch the computer on.
- Hold the programming wand over the pulse generator.
- From the Main Menu, select “Interrogate Device” (Interrogation is always the first and last step in a programming sequence).
With the wand placed over the pulse generator, select “Start Interrogation”

It can take up to 15 seconds for the interrogation to be completed and for the VNS generated settings to be displayed.
**Step 2: Program Patient Data**

- Check that the Patient ID and the date of surgical implantation have been entered and are correct. If not, program as necessary. This helps to review patient data stored within the handheld computer. Refer to section 2 for procedure.

**Step 3: Activation of the Device- should be at 0.25 on pictures**

- Explain the potential side effects of stimulation which may include a slight cough, throat discomfort and hoarseness. Reassure the patient any such symptoms should settle.
- Program initial settings by tapping the “New” button for the parameter you want to set i.e., Output Current & Magnet Current.

*Screenshots to demonstrate screen differences between models. Default output current would be 0.0mA

*See Appendix for explanation of settings
Possible switch on settings for 103/104/105

<table>
<thead>
<tr>
<th>Parameter name</th>
<th>Parameter</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Output Current</td>
<td>0.25mA</td>
<td>Switch on and assess tolerability</td>
</tr>
<tr>
<td>Signal Frequency</td>
<td>20-30Hz</td>
<td>May be lowered from 30 in the event of poor tolerance</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>250-500µsec</td>
<td>250 recommended for tolerability</td>
</tr>
<tr>
<td>On Time/Off time</td>
<td>7s On/ 1.8min Off OR 30s On/5min Off (Both 10% duty cycle)</td>
<td>Dependent on tolerability and efficacy</td>
</tr>
<tr>
<td>Magnet Output Current</td>
<td>0.5mA</td>
<td>Should be 0.25mA above output current</td>
</tr>
<tr>
<td>Magnet Pulse Width</td>
<td>250/500µsec</td>
<td>Can use either depending on tolerability/efficacy and output current pulse width</td>
</tr>
<tr>
<td>Magnet On Time</td>
<td>14 – 60s</td>
<td>Depending on tolerability</td>
</tr>
</tbody>
</table>

- Tap ‘New’ in the desired parameter
- Use scroll buttons to view more selections

(106 pictures- second pic incorrect setting with regard to initial settings)
• Select “Program”
• A confirmation screen will appear for you to check the desired parameter changes. Here you can modify these changes if needed or press confirm to go ahead.

Tap confirm to go ahead with the changes.

Once the generator has been programmed, the normal stimulation will be delivered.
• Check parameters are programmed and delivered as desired.
• Then undertake Systems Diagnostic test (see Section 6: Diagnostics).

• Undertake final interrogation. This is important to confirm the desired settings have been programmed safely.

• To close the session, select “Menu” followed by “Main Menu”, which returns you back to the very first screen. You can now switch the tablet off via the power button if your programming session has finished.

Step 4: Speed of Ramp Up

• If an output current of 0.25mA is usually very well tolerated at the first appointment, consideration can be given to increasing the output current to 0.5mA and the magnet current to 0.75mA within the same appointment. This may be particularly appropriate if the patient lives a long distance from the VNS clinic.

Step 5: Assessing Initial Response to Stimulation

• Allow time for two or three duty cycles to complete whilst still in clinic, to assess for any potential side effects and to reassure the patient/family/carers.

• If the patient finds the stimulation uncomfortable and is not reassured that the symptoms will settle, consider reducing the signal frequency to 25Hz (followed
by 20Hz) or pulse Width from 500µs to 250µs or changing to shorter on time (see Section 3: Management of Side Effects).

- Consider administering a magnet swipe in clinic to assess tolerability, if not tolerated consider a reduction in on time, Magnet output current or pulse width as necessary.

**Step 6: Patient Essentials**

- Give the patient the Patient Essentials pack which includes two magnets, the patient manual and the emergency information card.

- Demonstrate how to use the magnet in response to seizure activity (see Section 4: Magnet Use). Advise that this may not be effective whilst at low output settings.

- You may decide to demonstrate how to temporarily switch off the VNS generator by using the magnet.

- Supply the VNS therapy magnet booklet for epilepsy/ depression as appropriate.

- Provide information about how the patient can contact the VNS Clinic between appointments.
**Subsequent Appointments to Increase the Output (ramping up)**

At subsequent visits to the clinic, the patient should be encouraged to bring an up to date list of their medication and a seizure diary.

**Ramping up**

The treatment plan is to increase the VNS output and magnet currents to a therapeutic level at a speed tolerated by the patient. Slower ramp up speed may be considered for those considered vulnerable or who are non-verbal. Practice across the UK includes monthly, fortnightly, weekly ramp up and “rapid” ramp up over the course of a week. These programming schedules may be used as patient condition and tolerability dictates.

Ramp up of output current usually takes place in 0.25mA increments but this can be increased as tolerated, and an increase of 0.5mA is common in areas with geographical issues.

The therapeutic level of the VNS will vary between patients but will usually be between 1.5mA to 2.5mA, however, this may be lower in some individuals. Adjustments to VNS parameters should always be made taking into consideration efficacy and tolerability. If currents outside of these parameters are considered it may be beneficial to seek guidance from other programmers or LivaNova.

Magnet on time is usually 30-60 seconds however, other settings are available and can be effective (14, 21 seconds)

Magnet on time may be reduced if output current on time is short or if patient has short seizures or clusters of brief seizures

The following points should be considered at each appointment in the VNS clinic during the ramping up phase:

- Assess efficacy and tolerability of the VNS settings programmed at the last appointment including use of the magnet.
- Interrogate device, adjust VNS parameters as desired, perform system diagnostic test and re-interrogate the generator.
- Assess efficacy and tolerability of the VNS settings by observing the patient and activating the VNS with the magnet.
- It is important to identify any positive effect on seizure control and quality of life when it occurs so that changes to the VNS duty cycle can be considered instead of continuing to increase the output current. Positive changes can include:
• Seizure frequency
• Seizure duration
• Seizure severity
• Post-ictal Recovery Period
• Quality of Life
  o Alertness
  o Mood (+Depression)
  o Cognition
  o Improved sleep
  o Academic Ability
  o Verbal Skills
  o Memory

- Increases to output current are made subject to tolerability (see Section 3: Management of Side Effects). Most patients can tolerate a maximum output currents of 2.25/2.5mA.

- A system diagnostic test should be performed at every appointment to monitor the integrity of the VNS System. With the pulse generator model 102 this test should only be undertaken once the output current has reached an output current of at least 0.75mA signal frequency 15Hz and On time of 30 seconds. (See Section 6: Diagnostics for more information).

- Following each clinic appointment a letter should be sent to the patient and professionals involved in the patients care, for example, GP, paediatrician, neurologist, learning disability team, carers/family. This should outline the VNS settings, response to VNS therapy, current level of seizure activity, quality of life measures, regular anti-epileptic medication and rescue medication (see Appendix 2 for sample letter).

- It is recommended that changes to regular anti-epileptic medications are avoided wherever possible whilst the VNS parameters are being adjusted in order to allow the effect of VNS therapy to be assessed.

- It is advised that subsequent appointments are based on the individual needs of the patient and the availability within the VNS clinic.

- Care plans/protocols may be developed and disseminated where appropriate. This may need to be organised before implantation.
• It is recommended that total on time of the device and total number of magnet swipes is documented in patient records

**Adjustment of the Duty Cycle for 102/103/104/105**

**106 can be adjusted in a similar way but must have an off time of more than 1 minute**

First increase the output current of the VNS up to the therapeutic/tolerated range (Maximum output current of 2.5mA) then consider changing duty cycle.

The duty cycle can be adjusted by changing the Signal On and Off times. The usual starting duty cycle is 10% (7 sec on, 1.8 mins off OR 30 sec on 5 mins off). LivaNova DO NOT recommend using Duty Cycles where On Time is greater than Off Time

**VNS Duty cycles**

<table>
<thead>
<tr>
<th>On Time (Seconds)</th>
<th>Off Time (Minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>0.3 0.5 0.8 1.1 1.8 3 5 10</td>
</tr>
<tr>
<td>7</td>
<td>58% 44% 30% 20% 15% 10% 6% 4% 2%</td>
</tr>
<tr>
<td>14</td>
<td>69% 56% 41% 29% 23% 15% 9% 6% 3%</td>
</tr>
<tr>
<td>21</td>
<td>76% 64% 49% 36% 29% 19% 12% 8% 4%</td>
</tr>
<tr>
<td>30</td>
<td>81% 71% 57% 44% 35% 25% 16% 10% 5%</td>
</tr>
<tr>
<td>60</td>
<td>89% 82% 71% 59% 51% 38% 27% 18% 10%</td>
</tr>
</tbody>
</table>

**CAUTION:** Excessive stimulation at an excessive duty cycle (duty cycle for which the “On” time is greater than the “Off” time) has resulted in degenerative nerve damage in laboratory animals. This also can significantly deplete generator capacity
**VNS Duty Cycles.**

Duty Cycles can be a highly effective treatment option in maximizing the benefits of VNS Therapy. Variances in On and Off time (Duty Cycle) could be set to impact on specific seizure semiology. It is preferred to adopt a methodical approach to changes in Duty Cycle and LivaNova recommend a minimum of a 3 month period to assess efficacy and tolerability.

If a higher Duty Cycle has shown to be ineffective consider reducing to a lower Duty Cycle to preserve battery life.

Possible parameter aims of VNS therapy

<table>
<thead>
<tr>
<th>Parameter name</th>
<th>Parameter</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Output Current</td>
<td>1.5-2.5mA</td>
<td>As tolerability/efficacy</td>
</tr>
<tr>
<td>Signal Frequency</td>
<td>20-30</td>
<td>May be lowered from 30 in the event of poor tolerance</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>250-500</td>
<td>250 recommended for tolerability and to prolong battery</td>
</tr>
<tr>
<td>Duty cycle</td>
<td>10%-49%</td>
<td>Dependent on tolerability and efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NB Shorter off times may be beneficial for clusters of short seizures</td>
</tr>
<tr>
<td>Magnet Output Current</td>
<td>1.75-2.75</td>
<td>Should be 0.25mA above output current dependent upon tolerability</td>
</tr>
<tr>
<td>Magnet Pulse Width</td>
<td>250/500</td>
<td>Can use either depending on tolerability/efficacy</td>
</tr>
<tr>
<td>Magnet On Time</td>
<td>14 – 60s</td>
<td>Depending on tolerability</td>
</tr>
</tbody>
</table>
Section 4: MANAGEMENT OF STIMULATION RELATED SIDE EFFECTS

Patients may experience side effects related to VNS therapy. These may occur after the device is activated, following increases to the output current or changes to the duty cycle. Side effects which can be experienced include:

- Hoarseness
- Tingling Sensation / Pain / Discomfort in Throat
- Cough
- Dyspnoea
- Toothache
- Ear pain
- Jaw / Neck pain

Patients should be advised that these symptoms are generally short lived and will resolve or become tolerable within a short period of time.

Some patients can experience a period of breathlessness during VNS therapy. Therefore the patient may wish to consider switching the VNS off temporarily, using the magnet, immediately prior to taking exercise or public speaking.

If the side effects become intolerable the following measures can be programmed to alleviate any discomfort.

Assessment of Side Effects

It is important to establish if any symptoms are attributed to VNS therapy. Side effects that are related to VNS therapy may only occur whilst stimulation is being delivered. However, chronic pain or discomfort may be experienced which can be managed in the following steps:

Management of Side Effects

1. When VNS is established as a likely cause of side effects, the following is recommended:
   - Reduce signal frequency from 30 Hz to 25Hz or 20 Hz
   - And/Or
   - Reduce the pulse width from 500μsec to 250μsec.
   - And/Or
   - Change the duty cycle so the on time is shorter

A pulse width of 130 may be considered for a short time to alleviate symptoms but this is normally sub-therapeutic so the pulse width should be increased to 250 as
soon as possible. Patients should be counselled that this may cause a worsening of their therapeutic effect of the VNS.

Section 5: MAGNET USE

The VNS magnet pack (patient essentials kit) should be given to the patient when the VNS device is activated for the first time (see Section 2: Activation and Subsequent Programming).

The magnet serves 3 functions:

1. Activating the magnet stimulation mode will result in an extra dose of stimulation being delivered at the onset or during a seizure. This may have the effect of:

   • Stopping the seizure
   • Shortening the duration of the seizure
   • Reducing the seizure severity
   • Shortening the post-ictal period.

2. Some patients benefit from prophylactic usage of the magnet to prevent predicted seizure pattern such as during exercise, clusters, early morning seizures or periods of tiredness

3. Stopping stimulation to temporarily switch the device off if, for example, there are problematic side effects.

How to use the magnet during seizures
A swipe involves moving the magnet over the generator and can be done in the following ways for example, ‘criss cross’ method, swipe and remove, zig zag, etc. This should take no longer than 3 seconds This should be used as per individual care plan. This can be used effectively over a maximum of 2 layers of clothing.

Activating magnet stimulation will result in the generator delivering stimulation in accordance with the programmed magnet settings (see Section 2: Activation and Subsequent Programming). The magnet output current is usually set at 0.25mA higher than the output current.

Magnet stimulation should be activated by the patient as soon as possible after the onset of an aura. If no aura is experienced a carer can activate magnet stimulation as soon as possible after the onset of a seizure.

Magnet stimulation can be activated several times during a seizure if this is necessary and this will not harm the patient or the generator. However, patients and carers should be made aware that the magnet does not replace rescue medication and urgent medical assistance should still be summoned if required.

Magnet stimulation can be uncomfortable for patients who retain a degree of awareness during their seizure. If necessary, consideration can be given to reducing the magnet on time, magnet pulse width or magnet current although patients should be counselled that this may reduce the efficacy of the magnet stimulation mode.

Magnet can be used when the patient is considered vulnerable to seizures such as when pyrexial or tired to try to prevent worsening seizure frequency.

**How to use the magnet to switch the device off temporarily.**

- Hold or tape the magnet over the pulse generator. Whilst the magnet is in this position, the pulse generator will not deliver any stimulation. On removal of
the magnet, programmed settings will restart at the previously programmed settings. Please note that prolonged generator deactivation may lead to the patient experiencing increased seizure activity.

- The magnet may be switched off for people wishing to have no stimulation with vocal hoarseness such as for choir practice, talking on the telephone etc. Be advised that the longer the device is switched off the stronger the stimulation would feel when the magnet is removed. This also may have an adverse effect upon seizure frequency.

**Magnet Management**

- The magnet should be kept at least 25cms away from credit cards, televisions, computers, microwave ovens or any other magnets.

- The patient/carers should carry the magnet with them at all times so that it is available for immediate use (the Patient Essentials pack includes a wrist strap and belt clip).

- Patients/carers should be counselled that by wearing the magnet to bed they may accidentally activate the magnet stimulation mode or deactivate the generator.

- Ask the patient to monitor the effect of any magnet use.

- If the patient is concerned that the magnet stimulation mode is not functioning correctly, a magnet mode diagnostic test can be undertaken (see Section 6: Diagnostics).


Section 6: DIAGNOSTICS

The programming tablet can perform various diagnostic tests on the VNS system. These are accessed via the ‘Device Diagnostics’ tab (see below).

The ‘Device Diagnostics’ tab gives access to ‘System Diagnostics’ and ‘Other Diagnostics’ (see below).
Generator models 103, 104, 105 and 106

It is recommended that a System Diagnostics test should be performed at every VNS review. At the first appointment following implantation, the System Diagnostics test should be undertaken after the generator has been switched on. (Please note that if the generator has not been activated an initial system diagnostics test will be carried out at 1mA and the patient may experience some discomfort).

The System Diagnostic test evaluates the lead impedance of the VNS system as well as the generator's ability to deliver the programmed stimulation. The System Diagnostics test on generator models 103, 104, 105 and 106 will assess lead impedance, impedance value (measured in Ohms), output current and current delivered (measured in milliamps).

Normal mode diagnostics are not required on generators 103/104/105/106. These generators will run the system diagnostics at the programmed output current.
Lead Impedance & Impedance Value

The normal range for lead impedance is between 600 Ohms and 5300 Ohms. A lead impedance of 5300 Ohms or greater would be considered high. A lead impedance of 10000 Ohms or greater may be indicative of a lead discontinuity. A lead impedance of 600 Ohms or less would be considered too low and may also be indicative of lead discontinuity or a short circuit.

Any large changes in impedance values (over 1000 Ohms) may be significant and represent a potential problem with fibrosis, this should be documented and evaluated regularly. If impedance continues to rise Livanova should be contacted for advice.

Output Current & Current Delivered

A systems diagnostic test on a model 103, 104, 105 and 106 generator also gives us information regarding the ability to deliver normal stimulation.

When the programmed current is delivered the result is displayed as “OK”.

If the normal current cannot be delivered, this would display the message “LIMIT”. This would indicate that the current the generator was delivering was less than the programmed output current.

Warning of High Lead Impedance on Interrogation
The generator models 103, 104, 105, 106 automatically test lead impedance every 24 hours. If the lead impedance has been out of the normal range between VNS clinic appointments a warning message will be displayed upon interrogation of device (see below).

When this occurs, a system diagnostics test should be performed to confirm the warning message of possible high or low lead impedance. High lead impedance is indicated by a lead impedance of >=10000 ohms in generator model numbers 103, 104 and 105.

**Pulse Generator models 101, 102 & 102R**

**System Diagnostics Test**

The System Diagnostic test evaluates the lead impedance only. The impedance value is measured in DCDC. This tests the integrity of the system at an output current of 1mA, signal frequency 20Hz, pulse width 500µsecs regardless of the patients set parameters. This test should not be undertaken until the output current has been programmed to 0.75mA and is well tolerated at this level.

NB. If the programmed on time is less than 30seconds then the patient will need to be reprogrammed to 30 seconds in order to carry out the diagnostics test. This should always be reprogrammed afterwards.
A DCDC value of 0 to 3 is acceptable. A DCDC value of 4 to 7 equates to high lead impedance. This DCDC range will not give a low impedance indicator, however a reduction in DCDC values together with deterioration in seizure control could indicate a short circuit in the system. These cases are extremely rare.

An Output Status indication of ‘LIMIT’ would indicate that the 1mA output current is not being delivered.

Normal Mode Diagnostics Test 102 models only

This test should also be undertaken with generator models 101, 102 and 102R if the generator has been programmed with an output current greater than 0.75mA to establish whether the programmed output current is being delivered.

The Normal Mode Diagnostics test is accessed by tapping ‘Other Diagnostics’ on the programming handheld.
On a normal mode diagnostics the DCDC values can range from 0 to 6. A higher DCDC value shows that the generator is working harder to deliver the programmed output current. It is crucial to monitor the output status indicator as this determines if the therapeutic current can be delivered. A DCDC value of 7 usually coincides with Output Status: ‘LIMIT’ and this would indicate that the pulse generator is not able to deliver the programmed output current. This would require further investigation. Any high results will be highlighted in red.
**High Impedance for all devices**

High lead impedance could indicate possible:

- Fibrosis between the nerve and the lead
- Lead discontinuity
  E.g. Lead break, electrode detachment from the nerve or lead pin not fully inserted.
- Pulse generator at end of service

In this situation, it is advisable to take the following actions:

Switch off the generator (continuing stimulation with a fractured lead may result in dissolution of the conductor material resulting in pain, inflammation, vocal cord dysfunction). NB Switching off the device could lead to an increase in seizures that may require additional medication and the patient/carers/family should be counselled about the risk of SUDEP.

Obtain anterior-posterior (AP) and lateral chest and neck x-rays to visualise the lead and generator. For best results advise your radiology dept to have the plate perpendicular/face onto the generator.

Lead breaks are not usually seen on x-ray which cannot therefore exclude the presence of a lead break.

- Inform your regional LivaNova representative who will arrange for the x-rays to be reviewed and will offer advice.
Consider a surgical evaluation

Discuss the above with the patient/carer

Section 7: GENERATOR REPLACEMENT

Once the optimal VNS settings have been reached, patients should be reviewed at least every 6 months to check that the generator is working effectively and is not nearing End Of Service (EOS).

Once there is an Intensified Follow-up Indicator (IFI) warning message (feature 103/104/105/106), the patient should be assessed and, if appropriate, referred to the surgical team for a generator replacement.

It is well established practice that if the generator is at “IFI: Yes” and there is no imminent date for surgery, it may possible to reduce the output current and/or output current and/or pulse width to a minimum of 250µsec to prolong the generator capacity. This may lead to the generator no longer showing IFI as the device performs an automatic battery voltage measurement every 24 hours, and recalibration may then indicate that the device now has increased capacity, between 18-25% (see table below). If the pulse width is reduced it is recommended that the VNS is re-interrogated in a further 2-3 weeks to clarify the generator capacity and if surgery is required at this stage.

Example of broken lead.

Note: Not all broken leads show up on X-Ray such as micro-fractues

Patient consent given for X-Ray use
Please note any reduction in stimulation may lead to an increase in seizures which should be discussed with the patient and medication options be considered.

We recommend that.

In order to support your recommendation for surgery it would be useful to record:-

1. Two separate IFI readings with a minimum of 2 weeks apart. This is not always easy to arrange if the patient lives some distance from the hospital or if there is limited availability of clinic slots.
2. Total on hours
3. Total magnet activation

We would then recommend discussing the individual patient with your Livanova Territory Manager (contact details in Appendix 1) who may perform a battery life calculation to assess the longevity of the generator. Basic battery life calculations may be found in the back of the physician's manual for the relevant generator type.

An IFI demonstrates that the generator has between 8-18% capacity. A further reduction in its capacity will then indicate a Near End Of Service (NEOS) warning message. At this point the generator has between 0-8% capacity and LivaNova recommend urgent generator replacement to avoid the generator reaching End Of Service (EOS) and becoming disabled.

Once the generator has reached EOS it will no longer be providing any stimulation. It may also become impossible to interrogate or test the lead impedance of the device pre-operatively. In which case an X ray should be performed as suggested on page 34.

If replacement occurs before the original generator has reaches its end of service, the new generator can be activated during or shortly after surgery. This will minimize any discontinuation of therapy.

If VNS is activated in theatre ensure that a post-operative evaluation is carried out to assess patient comfort and tolerability.

Many practitioners consider activating the new generator between 0.25-0.50mA below the pre-operative settings, to avoid any potential discomfort as the patient adjusts to the new generator. If these settings are uncomfortable, reduce the output current to a lower level. This may result in an increase in seizures.

If the original generator reaches its end of service prior to replacement surgery, the output current will need to be gradually increased from 0.25mA as tolerated until a therapeutic level is reached.

Before theatre is scheduled it is essential to clarify whether the original VNS system have a single (102/103/105/106) or dual pin (101/102R/104) to ensure the correct product is available for replacement. See Appendix 4 for compatibility matrix.
The following is an illustration of progression of battery depletion for generators 103/104/105/106. How fast the battery depletes is dependent upon the generator settings. An estimation of these can be made from Battery Longevity Tables which are published on LivaNova.com under information on specific generator model manuals.

**IFI Activated (Intensified Follow-up Indicator)**
**Near End of Service**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>% Battery Charge</th>
<th>Battery Status Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;0 to 6%</td>
<td>N EOS = Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The N EOS has been triggered for the Generator.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The Programming Software will display a warning message indicating this status upon completion of interrogation or Diagnostics testing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>It is recommended that the Generator be replaced as soon as possible.</td>
</tr>
</tbody>
</table>

**End of Service**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>% Battery Charge</th>
<th>Battery Status Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0%</td>
<td>EOS = Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The Generator has reached EOS and is NOT supplying stimulation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The Programming Software will display a warning message indicating this status upon completion of interrogation or Diagnostics testing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediate replacement of the Generator is recommended.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If the Generator is not replaced, it will eventually lose the ability to communicate with the Programming Software.</td>
</tr>
</tbody>
</table>
For Models 101/102/102R

There is no visual representation of the battery. Upon interrogation the Near End of Service display at the bottom of the screen will either display YES or NO within approximately 3-6 months of total battery depletion. Again this time is dependent on the settings of the generator and an estimation can be made from Battery Longevity Tables which are published on LivaNova.com under information on specific generator model manuals.

Section 8: DEACTIVATION FOR LACK OF EFFICACY

If there has been no beneficial effect from VNS therapy at therapeutic dose, either seizure control or quality of life improvements, after a reasonable period of time (18 - 24 months at therapeutic dose is recommended) and various programming options have been tried, it would be reasonable to consider turning the VNS generator off for a trial period.

There is no recommended switch off protocol. If the generator is to be switched off, the options would be to:

- Gradually reduce the duty cycle and or output current over several appointments
- Switch it off immediately.

The VNS Device is switched off when the output current and magnet current are set to 0.00mA. If the magnet mode is helpful, the magnet stimulation can remain switched on at a tolerated setting to be used when required. NB. If the patient has infrequent seizures stimulation with the magnet could cause significant discomfort if the patient is aware during their seizures, this must be carefully considered.
The patient and family should be counselled that switching the device off may lead to an increase in seizures which may increase the risk of harm including SUDEP.

Once the device has been switched off, the patient should be reviewed after 3-6 months.

If their seizure controls worsens the patient may contact their VNS service to discuss switching the device on prior to the planned review date. It may also be worth considering switching the device on in other circumstances such as lower mood or reduced alertness. The device should be ramped back up to therapeutic range as tolerated.

The VNS device can remain in situ indefinitely whilst switched off. This is advantageous because it allows VNS therapy to be tried again at a later date. Also, advances in VNS therapy may become available.
Section 9: SWITCHING OFF FOR MRI

For full information about the compatibility of MRI with the VNS therapy system please refer to LivaNova guidance which your LivaNova representative will be able to provide. Decisions about whether to scan patients are the responsibility of the local radiology department.

- Any patient with a full VNS System requiring an MRI scan (1.5 or 3T) can be scanned using a transmit/receive type RF coil.
- Head and extremity (Ankles/knee) are permissible with a transmit and receive type of RF coil.
- Under no circumstances can a patient be scanned between the levels of C7 and T8 with a full VNS System in situ (new indication see below)
- If a patient has less than 2cm of lead remaining then a full body can be performed (New)

- If the Generator is explanted but part of lead remains.an MRI can still be performed using a Transmit and Receive Coil but not between C7 and T8 (New)
- If a lead break is present or suspected an MRI can still be performed using a Transmit and Receive Coil but not between C7 and T8 (New)

Contraindications for MRI;
- Patient has other implanted devices in addition to the VNS system.
- If the patient is scanned inappropriately it will heat the VNS system to dangerous levels which may lead to internal damage to the patient.
Pre-MRI:

1. Perform an interrogation and record the generator settings. This information is used to restore the device settings in case of a reset.
2. Perform System Diagnostics to ensure proper operation of the device. High or low impedance may indicate a potential Lead break.
3. Reprogram the Output Current parameter settings for both Normal Mode, Autostim and Magnet Mode as follows:
   - Output Current (mA): 0.0
   - Mag. Current (mA): 0.0
   - Autostim Off
4. Interrogate the device to verify programming was successful.
5. Verify that the placement of the VNS Therapy System is located between C7-T8.

Immediately before starting the MRI procedure, the patient should be instructed to notify the MR system operator of pain, discomfort, heating, or other unusual sensations so the operator can terminate the procedure, if needed.

Post-MRI:

1. Interrogate the VNS device.
2. If the Pulse Generator was reset during the scan, reprogram the serial number, patient ID, and Implant date as needed.
3. Program the patient’s therapeutic parameters as they were before the MRI procedure.
4. Perform System Diagnostics. Results should indicate Impedance = OK.
5. Interrogate the device again to confirm that reprogramming was successful.

It is important that the patient/family/carers are aware that there are restrictions on performing MRI scan.
Section 10: IN THE EVENT OF A PATIENT DEATH

It is advisable to discuss these sensitive issues with the family/patient/carers upon implantation where possible.

When a person receiving VNS therapy dies, the VNS generator will continue to stimulate for as long as the battery is working.

In the event of a patient death, LivaNova should be informed and will ask for a follow up form to be completed.

If acceptable to the patient’s family LivaNova would prefer to have the VNS device explanted and returned to them for review. Please contact your local representative and they can arrange this.

When possible and appropriate, the device can be removed by the hospital mortuary service or funeral director.

LivaNova will liaise with the appropriate person to arrange for the device to be returned to them in their product return kit which they will supply.

If a cremation is planned, the VNS generator should always be removed by the funeral director in advance of the cremation due to the risk of explosion.

If a burial is planned, the generator can be removed or left in situ for burial.
Section 11: AspireSR

10.1 What is AspireSR

AspireSR (Seizure Response) is the function of the Model 106 Generator to react to increasing heart rate associated with seizures, Ictal Tachycardia is shown to present in 82% of patients with epilepsy (Eggleston, K., Olin, B., Fisher, R. 2014)

10.2 Contraindications

- Vagotomy
- Diathermy
- Cardiac arrhythmia (Model 106 only)—The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias or who are using treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillator, beta adrenergic blocker medications).

10.3 Initial Settings

10.4 Verify Heartbeat

10.5 Seizure Detection Threshold

10.6 Autostimulation management of AspireSR

10.7 Duty Cycle Management

10.8 Analysis of Performance – Display Device History

10.9 Aspire SR Therapy Viewer

Note: VNS programmers should only programme 106 device if they have had training from LivaNova representatives or an experienced 106 programmer. Please contact your local LivaNova representative of Epilepsy Specialist Nurse with any queries.
10.3 Initial Settings

Caution: There is a software error called ‘Burst WatchDog’ If this occurs then the generator can reset all output currents to 0.0mA.

To avoid this it is important to make sure the Output Current for Autostim is ALWAYS less than the Output Current for the Magnet.

Switch on parameters for 106

<table>
<thead>
<tr>
<th>Parameter name</th>
<th>Parameter</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Output Current</td>
<td>0.25mA</td>
<td>Switch on and assess tolerability</td>
</tr>
<tr>
<td>Signal Frequency</td>
<td>20-30Hz</td>
<td>May be lowered from 30 in the event of poor tolerance</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>250-500μsec</td>
<td>250 recommended for tolerability</td>
</tr>
<tr>
<td>On Time/Off time</td>
<td>7s On/1.8min Off OR 30s On/5min Off</td>
<td>Dependent on tolerability and efficacy</td>
</tr>
<tr>
<td>Magnet Output Current</td>
<td>0.5mA</td>
<td>Should be 0.25mA above output current</td>
</tr>
<tr>
<td>Magnet Pulse Width</td>
<td>250/500μsec</td>
<td>Can use either depending on tolerability/efficacy</td>
</tr>
<tr>
<td>Magnet On Time</td>
<td>14 – 60s</td>
<td>Depending on tolerability</td>
</tr>
<tr>
<td>Seizure Detection</td>
<td>On/Off</td>
<td>Switch on in Theatre to Assess ability to identify seizures</td>
</tr>
<tr>
<td>Heart Beat Sensitivity</td>
<td>1-5 (Start at 1) (Usual setting is 1-3)</td>
<td>Start at 1 and work through levels until accurate heart rate identified (within ±5 BPM)</td>
</tr>
<tr>
<td>Seizure Detection Threshold</td>
<td>20-70% (Usual practice is to start at 40%)</td>
<td>Start at 40% and aim for 20% for more efficacy. For tolerability reasons change from 40% to 50%,60% or 70%</td>
</tr>
<tr>
<td>Autostim Output Current</td>
<td>0.375mA</td>
<td>Never have equal to Magnet. Utilize middle step between normal mode and Magnet Mode where possible</td>
</tr>
<tr>
<td>Autostim Pulse Width</td>
<td>250-500μsec</td>
<td>Generally Keep the same as Normal Mode for tolerability</td>
</tr>
<tr>
<td>Autostim On Time</td>
<td>30 or 60 secs</td>
<td>Depending in tolerability and efficacy</td>
</tr>
</tbody>
</table>
10.4 Verify Heart Beat

It is important that the AspireSR generator reads the correct heart rate. This is calibrated manually and is normally checked in the Operating Theatre after the initial system diagnostic is performed. Although not specifically recommended by LivaNova it is prudent to check this is calibrated correctly once every 6 months.

The AspireSR has 5 programmable settings (1-5) for Heartbeat Detection (sensitivity), which can be programmed.

- Default settings for Heartbeat Detection is 1.
- HB1 = least sensitive setting
- HB5 = most sensitive setting

In the above illustration, the 3 large peaks represent R waves from the PQRST complex. The smaller spikes represent artefact

- If HB 1 was selected then AspireSR would undersense the heart rate,
- If HB 5 was selected then AspireSR would over sense as it would pick up artefact.

In this example HB 3 should be used

LivaNova recommend a Pre-surgical Surface assessment in order to programme heartbeat settings, however, this is rarely used in clinical practice. It is recommended in patients who have unusual positioning of generator. If not available, start with 1 and increase until accurate heartbeat is detected and displayed stable.
Programming Steps

After the “Seizure Detection” is enabled, the Verify Heartbeat Detection button becomes active

If this is enabled for the first time, or after each change of Heartbeat Sensitivity the Heartbeat Detection Feature will run automatically

Step-by-Step procedure:

1/ Interrogate the Model 106 device
NB. If VNS is stimulating at time of testing display will show ---- or ????, allow stimulation to finish and then continue

2/ Navigate to the Seizure Detection tab of the Parameters screen. Turn Seizure Detection On. Select Program.
3/ Confirm settings then Start Programming; a reminder to hold wand over the generator will be displayed.

4/ Select Proceed and the software will immediately begin the Heartbeat Detection.

5/ Immediately after the programming is complete, while the wand is held over the Model 106 device, the Screen displays:

- Currently programmed Heartbeat Detection Sensitivity
- A countdown from 120 until 0 seconds
- The heart rate as detected by AspireSR in the BPM window (Beats per minute)
- Let this run for at least 15-20 seconds for the BPM value to stabilize.
6/ Measure the patient’s pulse, or obtain the patient’s heart rate using a different heart rate monitor and compare this value against the BPM value recorded in Step 5. The two BPMs should be approximately equal in value (±5 BPM).

In addition to numerical values, three other visual indicators may be displayed in the BPM window:

????? or ***** indicates that the detected BPM is out of range. If this happens then alter the HB sensitivity. As mentioned previously you may also get this result if the device is currently stimulating.

----- is displayed in the BPM window when the Verify Heartbeat Detection feature is OFF.

If the reported heart rate (BPM) appears to be too high/low, or if ???? or ***** is displayed, exit the screen by tapping on Stop and then Exit whilst the wand is over the device.

Then reduce/increase the Heartbeat Detection sensitivity, program and reassess heartbeat detection performance from seizure detection tab.
10.5 Seizure Detection Threshold

The seizure detection threshold is the percentage change in heart rate over a short period of time in which the device detects what is a heart rate increase which could be associated with a seizure and delivers automatic stimulation.

The Threshold for AutoStim offers 6 sensitivity levels (20-70%) for triggering an automatic stimulation.

- Most sensitive is 20%
- Least sensitive is 70%

Default settings for Threshold for AutoStim is 70%. Common practice suggests to initially change this to 40% and adjust according to clinical response. A Threshold of 20% is likely to respond quicker to a seizure but assess patient's tolerability to this. See graph below from regulatory data.
To change the Threshold for Autostim this is accessed under the seizure detection tab (see below)
10.6 Autostimulation management of AspireSR

Efficacy of Aspire SR is gained by assessing clinical response in conjunction with the AspireSR Therapy Viewer (Autostim history on tablet) and adjusting the following parameters in conjunction with Normal Mode and Magnet Mode stimulation

- Autostim Output Current
- Threshold for Autostim

*Autostim output* is recommended to be 0.125mA above Normal Mode and 0.125mA below Magnet Mode.

From 2mA and above the 0.125mA increment is not available so always keep Autostim at a current less than the magnet (this may be equal to or above the normal output current) due to the software error mentioned previously (Burst Watchdog).

As with normal mode parameters do allow for individual variation and tolerance

*Threshold for Autostim* is recommended at an initial setting of 40% and to be activated the same day as implantation. Threshold may be altered depending upon patient response and tolerability.

It is best practice to document the number and % of autostims at each office visit, this can be accessed via the “Display device history”.
10.7 Duty Cycle Management

When the seizure detection feature is enabled, certain Duty Cycles become unavailable. This is due to the time period needed for AspireSR to calculate algorithms and listen for Heart Rate changes (1 Minute). The boxed out area below shows Duty Cycles which are not available

For initial implants it is suggested to start at 10%. With Autostim activated this may mitigate the need to change the Duty Cycle but be prepared to increase the Duty Cycle still based on clinical response

For replacement implants this will be present a challenge should patients be programmed on settings not allowed by SR. For these patients it is suggested to assess whether AspireSR would give additional benefit eg if a patient is already seizure free there would be no need to switch it on.

For those patients on settings not compatible with auto-stimulation discussion should take place regarding future management options.
10.8 Analysis of Performance – Display Device History

One of the facilities to view the performance of AspireSR can be viewed via Display Device History as shown below.

Here a summary of the devices current settings can be found as shown below.

<table>
<thead>
<tr>
<th>Device Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Settings:</td>
</tr>
<tr>
<td>Output Current</td>
</tr>
<tr>
<td>Pulse Width</td>
</tr>
<tr>
<td>On Time</td>
</tr>
<tr>
<td>Magnet Settings:</td>
</tr>
<tr>
<td>Magnet Output Current</td>
</tr>
<tr>
<td>Magnet Pulse Width</td>
</tr>
<tr>
<td>Magnet On Time</td>
</tr>
<tr>
<td>AutoStim Settings:</td>
</tr>
<tr>
<td>AutoStim Current</td>
</tr>
<tr>
<td>AutoStim Pulse Width</td>
</tr>
<tr>
<td>AutoStim On Time</td>
</tr>
<tr>
<td>Configuration Settings:</td>
</tr>
<tr>
<td>Seizure Detection</td>
</tr>
<tr>
<td>Threshold for AutoStim</td>
</tr>
<tr>
<td>Heartbeat Detection (sensitivity)</td>
</tr>
</tbody>
</table>
Also a summary of the stimulation profile can be observed shown below

<table>
<thead>
<tr>
<th></th>
<th>Avg. Stims per Day</th>
<th>% per Day</th>
<th>% Therapy Time Since previous office visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>AutoStim</td>
<td>26</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>Magnet Stim</td>
<td>5</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Normal Stim</td>
<td>242</td>
<td>90%</td>
<td>9%</td>
</tr>
<tr>
<td>Total</td>
<td>273</td>
<td>100%</td>
<td>10%</td>
</tr>
</tbody>
</table>

This should be documented in patient records and letter.

Normal Stimulation Duty Cycle can decrease due to Autostim taking its place. The Total column gives the overall Duty Cycle contribution including SR stimulation

SAVE OFFICE VISIT if you want to recall this data on the tablets

Extended Generator Memory Download

The AspireSR generator offers the possibility to download the exact date and time the Autostim feature stimulated (Extended Generator Memory Download) To analyse this you will need an SD card reader and AspireSR Therapy Viewer available via a Microsoft Excel file

*A step by step guide can be printed viewed and printed off in Appendix*

**10.9 AspireSR Therapy Viewer**

To view the AspireSR therapy in a graphical from you will need the AspireSR Therapy viewer excel file which can be obtained from your local representative

The AspireSR Therapy Viewer can give an overview of the patient’s Autostim profile. The example below shows a histogram of the last 250 autostimulations,

*See Appendix 6 on how to perform the downloads*
It is also possible to view autostimulations on a daily basis. See example below, we can see a dominant area between 20.00-21.00 which stands out compared to the background.

This can be further scrutinized by using the tab which allows individual hours to be viewed as seen in example below.

Suggestions on using the AspireSR Therapy Viewer:

- Using the AspireSR Therapy viewer in conjunction with an accurate seizure diary can give a strong argument as to the effects of AspireSR.
• If Autostim logs correlate with seizures but no apparent response is observed then consider the following:
  - Are the seizures shorter, less intense or have an improved recovery period?
  - For improved efficacy consider adjusting the seizure detection threshold to be more sensitive eg 40% to 30% or 20%.
  - Consider increasing the Autostim output current (remember Autostim output current must be less than the magnet current)
If patterns cannot be observed consider it can take just one Autostim to prevent a seizure, unless the patient is observed constantly in Video Telemetry it can be difficult to prove an effect
• False positives can be ruled out by assessing if the autostimulations correlate with known time periods of exercise/activity
Appendices

Appendix 1: Livanova Contact Details

Steph Bolton - UK Area Manager
steph.bolton@livanova.com
07982 244510

Sally Brierley - North England
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Gloucester,
GL3 4AH.
01452 638 516

Freephone Clinical Technical Support
0800 046 1355
Appendix 2: Sample VNS Clinic Letter

Clinic date: 01/01/2014
Date typed: 01/01/2014

MEDICAL IN CONFIDENCE

Dr GP
The GP Practice
Anytown

Dear Dr,

Re: NAME – HOSPITAL NUMBER – DOB - ADDRESS

VAGUS NERVE STIMULATOR (VNS) REVIEW

<table>
<thead>
<tr>
<th>VNS Details</th>
<th>Parameters</th>
<th>VNS Settings</th>
<th>Adjustments made today</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model No. 103</td>
<td>Output current</td>
<td>0.5mA</td>
<td>1.0mA</td>
</tr>
<tr>
<td>Serial No. *****</td>
<td>Signal frequency</td>
<td>30Hz</td>
<td></td>
</tr>
<tr>
<td>Implanted:dd/mm/yyyy ID: ***</td>
<td>Pulse width</td>
<td>500µsecs</td>
<td></td>
</tr>
<tr>
<td>Efficacy: Not yet established</td>
<td>Signal on time</td>
<td>30secs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Signal off time</td>
<td>5mins</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnet current</td>
<td>0.75mA</td>
<td>1.25mA</td>
</tr>
<tr>
<td></td>
<td>Magnet on time</td>
<td>60secs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnet Pulse Width</td>
<td>500µsecs</td>
<td></td>
</tr>
<tr>
<td>System test: output status OK, lead impedance OK, Impedance Value 2000 Ohms, IFI: No Magnet swipes 17 (3 swipes since last review 6 weeks ago); Battery: 100%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Current Situation
I met with this gentleman in the VNS Clinic. He is going through a period of improved seizure control with his last seizure occurring around 4 weeks ago. His seizure diary shows that he normally has around 1-3 seizures each month.

Anti epileptic Medication and rescue medication

VNS Settings
He is tolerating the regular VNS stimulation well and is not experiencing adverse effects. There is some mild hoarseness during period of stimulation but this is not troubling.

We increased the VNS output current as outlined above which was well tolerated whilst he was in clinic. A device diagnostic check showed the pulse generator to be working well and not nearing its end of service.

Follow up
We have arranged to meet again in the VNS Clinic in 6 weeks at which time we will consider further increasing the output current.
Yours sincerely

Name
Epilepsy Specialist Nurse
Appendix 3: Pulse Width & Signal Frequency

Pulse Width

Pulse Width is measured in microseconds (µsec) and represents the duration of a single pulse during stimulation.

- If the patient cannot tolerate a pulse width of 500µsec, consideration can be given to reducing the pulse width to 250µsec

Signal Frequency

Signal Frequency is measured in Hertz (Hz) and represents the repetition rate of pulses (number per second) during stimulation.

- If the patient cannot tolerate a signal frequency of 30Hz, consideration can be given to reducing the signal frequency to 20Hz
## Appendix 4: Product Compatibility Matrix

<table>
<thead>
<tr>
<th>Pin Type</th>
<th>101</th>
<th>102</th>
<th>102R</th>
<th>103</th>
<th>104</th>
<th>105</th>
<th>106</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td>Single</td>
<td>Dual</td>
<td>Single</td>
<td>Dual</td>
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<td>✓</td>
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<td>✓</td>
</tr>
<tr>
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<td>✓</td>
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## Generator Replacement Matrix

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<th>Replacement Options</th>
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<th>102</th>
<th>102R</th>
<th>103</th>
<th>104</th>
<th>105</th>
<th>106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Generator</td>
<td>Dual</td>
<td>Single</td>
<td>Dual</td>
<td>Single</td>
<td>Dual</td>
<td>Single</td>
<td>Single</td>
</tr>
<tr>
<td>101</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>102 Pulse</td>
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<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
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<tr>
<td>102R Pulse Duo</td>
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<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>103 Demipulse</td>
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<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
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<tr>
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<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
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<td>105 AspireHC</td>
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<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>106 AspireSR</td>
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<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
Appendix 5: TROUBLESHOOTING

Unable to interrogate the Generator

- Check the connections from the programming computer to the wand.
- Check white connector and change as necessary
- Check the programming computer is disconnected from mains and is away from potential interference (i.e. other computers and mains operated devices).
- Ensure that the programming wand remains in place over the pulse generator during interrogation, i.e. at one location for at least 10 seconds.
- Assess the programming wand battery by simultaneously pressing and releasing the two red “Reset” buttons. Check that the green power LED light comes on:
  - If the light is on for more than 25 seconds this indicates sufficient battery life
  - If the light is on for less than 25 seconds, replace 9 volt alkaline battery of reputable brand, and ensure the internal connecting wires to the battery are not kinked. This may prevent the wand functioning.
- If the wand battery has sufficient life, consider if the VNS generator has reached its end of service.
- If problems persist, contact your LivaNova regional representative.
Appendix 6: VNS Therapy Motion Tablet

- The latest programmer, the motion tablet will work with all models of generators
- The old handheld programmers, Dell Axim X5 and X50 will work with all models of generators except Model 106, AspireSR. Contact your local LivaNova Manager should you require an upgrade

*US Version plug illustrated here
Appendix 7: AspireSR Therapy Viewer

To obtain the AspireSR Therapy analysis, 2 separate downloads need to be made
1/ Time and date of auto stimulations from the generator
2/ Time and date of last 15 Magnet Activations

First, decide via the ‘Display Device History’ option, decide how many records you need to download. Each number represents 1 autostim. The amount available to download is preset starting at 250 and increasing in increments of 250 up to a maximum of 4,096.

<table>
<thead>
<tr>
<th></th>
<th>Avg. Stims per Day</th>
<th>% per Day</th>
<th>% Therapy Time Since previous office visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>AutoStim</td>
<td>26</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>Magnet Stim</td>
<td>5</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Normal Stim</td>
<td>242</td>
<td>90%</td>
<td>9%</td>
</tr>
<tr>
<td>Total</td>
<td>273</td>
<td>100%</td>
<td>10%</td>
</tr>
</tbody>
</table>

In this example, if the patient had a seizure 17 days ago and wanted to see if the autostim stimulated then:
17 x 26 = 442.
Then it would be necessary to download 500 autostimulations in order to view that event.

Downloading time and date of autostimulations

- Verify that a SD card is inside the tablet and that the tablet time and date are set as accurately as possible
- Interrogate the Model 106 device.
- Select Menu from the Parameters screen, then select Admin Menu
Adjust the number of records to download by pressing the box containing 4096. The default 4096 may take up to 20 minutes. When ready, hold the wand over the Model106 device and select Start. Note that a time estimate for the interrogation is displayed.

Hold wand over the Model 106 Generator and wait for download of seizure detection records to complete.

After the download is complete, the records are saved onto the SD card in .cybx (csv) format and not displayed on the tablet screen.

2/ Exporting Autostimulation downloads

- Go back to the very first menu on the tablet and choose User ‘preferences’
- Press Database Utilities
- Press Export Database as text
Now open the AspireSR Therapy Viewer from the Excel File obtained from LivaNova

Under the ‘Start Here’ tab

Press ‘Click Here to View AspireSR Therapy’

Identify the required download (Hint: use serial number, date and time for ID)

Graphs will automatically be populated once you have clicked on the required file
Appendix 8: MRI Labelling (LivaNova Leavepiece)

MRI can be safely performed on patients with VNS Therapy provided that specified guidelines are followed.

VNS Therapy System
The VNS Therapy system (generator and lead), usually located between C7 and T8 vertebrae, must not be exposed to the radio frequency (RF) field.

MRI Zone
- with local Transmit/Receive coil

MRI Exclusion Zone
- Local Transmit/Receive coil commercially available

Note: Imaging techniques such as x-ray, computed tomography, and ultrasound are safe to perform in the MRI exclusion zone.
Performing MRI is safe when the guidelines below are followed

<table>
<thead>
<tr>
<th>Allowable imaging zones</th>
<th>See graphic on front cover</th>
<th>Full body</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF coil type</td>
<td>Head or local ONLY</td>
<td>Any</td>
</tr>
<tr>
<td>RF coil mode</td>
<td>Transmit/receive ONLY</td>
<td>Any</td>
</tr>
<tr>
<td>Static magnetic field</td>
<td>3T or 1.5T</td>
<td>3T or 1.5T</td>
</tr>
<tr>
<td>MRI configuration</td>
<td>Closed-bore</td>
<td>Closed-bore</td>
</tr>
<tr>
<td>MRI operating mode</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Spatial gradient field</td>
<td>≤720 gauss/cm</td>
<td>≤720 gauss/cm</td>
</tr>
<tr>
<td>Head-averaged SAR</td>
<td>≤3.2 W/kg</td>
<td>≤5.2 W/kg</td>
</tr>
</tbody>
</table>

*Equivalent to clipping the lead at the anchor tether

### Additional MRI considerations

- Only the implanted VNS Therapy system components are safe for MRI. All other VNS Therapy components (e.g., programming wand, programming computer, patient magnet) are MRI unsafe and must not be brought into the MRI scanner room.

- A transmit RF body coil can only be used if the VNS Therapy system has been removed and ≤2 cm of lead remains in the body. Surgical removal of the VNS Therapy system will be required if it is necessary to perform MRI using a transmit RF body coil.
Pre-MRI Instructions

An appropriate healthcare professional with access to a VNS Therapy programming system must prepare the VNS Therapy generator before the patient enters an MR system room.

✓ Interrogate the VNS Therapy generator* and record the generator settings.
✓ Perform System Diagnostics to ensure proper operation of the generator.
✓ Reprogram the Output Current parameter settings for Normal Mode, Magnet Mode, and AutoStim Mode* as follows:
  • Output Current (mA): 0.0
  • Magnet Output Current (mA): 0.0
  • AutoStim Output Current (mA): 0.0 and Seizure Detection "OFF"
✓ Interrogate the generator* to verify that programming was successful.
✓ Verify that placement of the VNS Therapy system is located between the C7 and T8 vertebrae.
✓ Instruct the patient to notify the MR system operator of pain, discomfort, heating, or other unusual sensations so the operator can terminate the procedure, if needed.

Post-MRI Instructions

After the MRI procedure, an appropriate healthcare professional with access to a VNS Therapy programming system should assess the condition of the VNS Therapy system.

✓ To assess the VNS Therapy system:
  • Interrogate the VNS Therapy generator
  • If the generator was reset during the scan, reprogram the serial number, patient ID, and implant date, as needed.
  • Program the patient’s therapeutic parameters as they were before the MRI procedure.
  • Perform System Diagnostics. Results should indicate impedance=OK
  • Interrogate the generator again to confirm that reprogramming was successful.
Appendix 9: Interaction with Other Devices, Interventions, Environment

Certain medical interventions, concomitant devices and environmental factors may interact with VNS. This is not an exhaustive list, please seek advice from LivaNova should you have any doubts.

_common:

Airport Security:

There is not expected to be any interaction or detection with airport scanners. Patients are advised to walk through normally but show their ID card supplied with the magnets should they need to

Electrocautery:

There is the possibility for electrocautery to damage the Pulse Generator. Between Bipolar and Monopolar electrocautery, Bipolar is the preferred safer option but should not be used in the immediate vicinity of the generator

If monopolar should be used then care must be taken to position the Earthing plate in a position as to direct the current away from the generator

Surgical Procedures:

*It is at the discretion of the anaesthetist and surgeon should they want to switch the device off*

X-Rays and CT Scans:

Both are safe with VNS

Less Common:

Cardiac Pacemakers:

Other implanted devices should be implanted 10cm apart from the VNS generator. Advice should be sought on the effect of magnets on the concomitant device> Aspire SR is contraindicated in those with a clinical meaningful arrhythmia

Defibrillation:

Care should be taken to position paddles away from generator if possible. If patient has been defibrillated do follow up with a system diagnostic to confirm functionality
Electromagnetic Induction Hobbs:
Although not formally studied there is the potential for the cooker to interact with the device if the patient is in the unlikely position of being directly above the hobb.

iPads:
Both the speaker and magnetic case sometimes used with ipads can cause magnet activations or temporary device switch off if held in position very close to the generator. It is advised to keep at least 10cm from the device

Lithotripsy:
There is the potential for high energy therapeutic treatments such as lithotripsy to damage the device. Care should be taken not to position the device in the path of the therapeutic intervention

Mammography:
This is safe with VNS in situ although care should be taken that VNS does not impede the view and analysis

Radiation Therapy:
Long term effects are unknown regarding the safety of radiotherapy although there is theoretical risk of a cumulative effect.

Ultrasound:
Diagnostic ultrasound is safe with VNS
Further Reading/References


GLOSSARY

AspireSR
Model 106 generator which features the Autostim functionality for seizures associated with Ictal Tachycardia

AspireSR Therapy Viewer
Microsoft Excel programme which allows viewing of autostimulation events

Autostim
Current delivered in response to increasing heart rate surpassing a defined threshold by the Model 106/AspireSR

BOL
Beginning of life

Duty cycle
Percentage of time during which stimulation occurs; stimulation time (programmed ON time plus 2 seconds of ramp-up time and 2 seconds of ramp-down time) divided by the sum of signal ON and OFF times

Electrode
Mechanical and electrical interface of the VNS Therapy System to the vagus nerve; part of the Lead

EMI
Electromagnetic interference

EOS
End of service

ERI
Elective replacement indicator

Excess duty cycle
Duty cycle for which the ON time is greater than the OFF time

High Lead impedance
Resistance to the flow of output current produced by the Pulse Generator, caused by any of the following: possible fibrosis between the nerve and electrode, dry nerve (during surgery), Lead fracture, Lead disconnection from the Pulse Generator, or high battery impedance approaching end of service

Heart Beat Sensitivity
1 to 5 scale in which the patient’s actual heart rate is manually calibrated

Lead
An implantable part of the VNS Therapy System; delivers electrical impulses from the Pulse Generator to the electrodes attached to the vagus nerve; contains flexible conductive wires within a bio-compatible insulating sheath

LIMIT output current
Output current other than that which was programmed; not a sole indicator of a device malfunction

Low Lead impedance
Lower than expected resistance to the flow of output current produced by the Pulse Generator potentially caused by a shortcircuit condition resulting from a break within the Lead body or connector boot

Magnet Mode activation
Brief Magnet application and removal, which initiates a stimulation

Output current
Amount of electrical current delivered in a single pulse of a stimulation, measured in milliamps (mA)
Pulse Generator
An implantable, multi-programmable part of the VNS Therapy System; generates electrical impulses that are delivered through the Lead to the vagus nerve; housed in a hermetically sealed titanium case and powered by a single battery.

Pulse width
Duration of a single pulse within a stimulation, measured in microsecond (µsec).

Radio frequency (RF)
Used in MR systems during the imaging process; also responsible for heating of the patient during MRI; the VNS Therapy System Lead, when exposed, can focus strong RF energy fields, such as those used during MRI, and cause excessive heating and possible injury.

Ramp-down
Gradual decrease over approximately 2 seconds in output current at the end of stimulation greater than 10 Hz in signal frequency.

Ramp-up
Gradual increase over approximately 2 seconds in output current at the beginning of stimulation greater than 10 Hz in signal frequency.

SAR (specific absorption rate)
A measure of RF power deposition in the MRI patient, usually expressed in watts per kilogram (W/kg).

Seizure Detection Threshold
Percentage change in heart rate at which the AspireSR delivers automatic stimulation.

Signal frequency
Repetition rate of pulses in a stimulation; measured in number of pulses per second (Hz).

Signal OFF time
Interval between stimulations when there is no stimulation, measured in minutes.

Signal ON time
Length of time the programmed output current is delivered (not including ramp-up and ramp-down times); measured in seconds.

Spatial gradient field
The change in the static magnetic field strength with respect to distance, usually expressed as Gauss/cm.

Static magnetic field strength
Strength of the static magnetic field used by an MR system for MRI, usually expressed in Tesla (e.g., 1.5-T, 3-T).

Statistically significant
Results are considered statistically significant if p-values for the appropriate statistical tests are less than or equal to 0.050.

Stimulation parameters
Programmed output current, signal frequency, pulse width, signal ON time, and signal OFF time.

Stimulation time
Therapeutic output of the VNS Therapy Pulse Generator; consists of the signal ON time, plus 2 seconds of ramp-up time and 2 seconds of ramp-down time.

SUDEP
Sudden unexplained death in epilepsy.

Transmit and receive RF head coil
A local imaging coil that both supplies RF energy and receives resonance signals during MRI procedure

Vagus nerve
Either of the pair of tenth cranial nerves arising from the medulla and supplying mainly the viscera, especially with autonomic sensory and motor fibers

VNS
Vagus Nerve Stimulation

VNS Therapy®
VNS delivered by LivaNova' VNS Therapy System