Vagus Nerve Stimulation Therapy System: 
In Vitro Evaluation of Magnetic Resonance 
Imaging-Related Heating and Function 
at 1.5 and 3 Tesla

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ABSTRACT

Objectives. To evaluate magnetic resonance imaging-related (MRI-related) heating for the VNS Therapy System at 1.5 and 3 tesla (T) using various device configurations and MRI conditions and to assess device function before and after MRI.

Methods. The VNS Therapy System (pulse generator, Model 102; leads Models 300 and 302; Cyberonics, Inc., Houston, Tex, USA) underwent assessment of MRI-related heating at 1.5 and 3 T using different positioning configurations, leads, transmit radiofrequency (RF) coils (body and head), RF power levels, and scans on different body regions. The function of the VNS Therapy System was evaluated before and after scanning.

Results. At 1.5 T using a transmit RF body coil, excessive temperature changes were associated with scans of the C-spine/shoulder (+11.5°C, complete system; +29.5°C, lead without pulse generator). The lowest temperature change occurred for the scan of the L-spine. At 1.5 T using a transmit/receive RF head coil, temperature changes did not exceed +0.2°C under the conditions studied. At 3 T using a transmit RF body coil, the highest temperature change occurred with the scan of the C-spine/shoulder (+14.5°C) with the lead configured with no strain relief loops at the vagus nerve. MRI performed using various conditions at 1.5 and 3 T produced no significant alterations in the function of the VNS Therapy System.

Conclusions. MRI-related heating was characterized for a variety of scenarios, identifying unsafe as well as safe conditions. Device function was unaffected by MRI procedures at 1.5 and 3 T. By following specific conditions, safety guidelines for the VNS Therapy System may be expanded beyond those currently indicated by the manufacturer.

KEY WORDS: magnetic resonance imaging, safety, vagus nerve stimulation

INTRODUCTION

Vagus nerve stimulation (VNS) therapy is a technique whereby a pulse generator is used to deliver intermittent electrical pulses via electrodes placed
on the left vagus nerve at the cervical level (1). VNS is an approved treatment for epilepsy and treatment-resistant depression and is under investigation as a therapy for other disorders, including anxiety, Alzheimer disease, morbid obesity, and migraine headaches (1,2).

Magnetic resonance imaging (MRI) is often needed to manage patients with the VNS Therapy System and has been utilized to elucidate the mechanisms responsible for the success or failure of VNS (3–5). Importantly, to ensure the safe use of MRI in patients with this device, scanning may only be performed by following specific guidelines. The product labeling states (6): “Magnetic resonance imaging (MRI) should not be performed with a magnetic resonance body coil. The heat induced in the lead by an MRI body scan can cause injury. If it is necessary to perform an MRI, only a transmit and receive type of head coil should be used . . . Thus, protocols must not be used which utilize local coils that are RF receive-only, with RF-transmit performed by the body coil. Note that some RF head coils are receive-only, and that most other local coils, such as knee and spinal coils, are also RF receive-only. These coils must not be used in patients with the VNS Therapy System.” These guidelines apply to MR systems operating at \( \leq 2 \) tesla (T) and a specific absorption rate (SAR) of \(< 1.3 \) W/kg. The rationale for these recommendations is that, similar to other neurostimulation systems (7–10), MRI-related heating is the primary safety concern for this device.

Safety recommendations for the VNS Therapy System are limiting patients for the following reasons: 1) many present-day 1.5 T scanners use a transmit RF body coil and a receive-only head coil to image the head/brain, not a transmit/receive head coil; 2) the utilization of 3-T MR systems for MRI examinations is increasing, therefore, safety needs to be assessed with regard to MRI-related heating at 3 T; and 3) the current labeling does not provide guidance for other body parts, which prevents this important diagnostic modality from being used to manage patients with conditions unrelated to the head/brain.

Investigations are needed to characterize MRI-related heating for the VNS Therapy System to determine if guidelines can be safely expanded to include the use of a transmit RF body coil and receive-only head coil, along with the ability to perform MRI examinations at 3 T. [With respect to the RF coil issues, it should be noted that MRI-related heating of implants tends to be substantially less when using a transmit/receive head or transmit/receive extremity coil compared to a transmit body coil because the overall area subjected to RF energy is minimized and the SAR level for a given pulse sequence is inherently less (7,9–11).] Furthermore, there is a need to determine if different MRI scenarios alter the functional aspects of the VNS Therapy System. Therefore, this investigation evaluated MRI-related heating for the VNS Therapy System at 1.5 and 3 T using various RF coil configurations and anatomic regions for MRI examinations and assessed the function of this device before and after MRI.

**METHODS**

**VNS Therapy System**

The VNS Therapy System (Cyberonics Inc., Houston, Tex, USA) consists of an implantable pulse generator (PG), a VNS therapy lead, and an external programming system that is used to change stimulation settings (6). (Note: the programming system was not subjected to MRI conditions.) The PG, Model 102, is an implantable, multiprogrammable device hermetically sealed in a titanium case with a polyurethane, single pin receptacle. For the MRI safety testing of the VNS Therapy System, PG normal mode output current was programmed to 0 mA and the magnet mode output current was programmed to 0 mA, according to recommendations provided by the manufacturer (6). Two different VNS therapy leads were assessed in this study: Model 300 (dual-pin connector) and Model 302 (single-pin coaxial connector). Both leads have a length of 43 cm and an outer diameter of 2 mm. These leads are made from MP35N wire insulated by silicone. The electrodes are platinum iridium. Each lead has one end that connects to the pulse generator with the other end containing three helical connections to the vagus nerve, as follows: a negative electrode (distal end), a positive electrode, and a nonconductive anchor tether, which is used to ensure secure placement on the left vagus nerve. This is the only neurostimulation system approved by the U.S. Food and Drug Administration for vagus nerve stimulation.
Phantom and Experimental Setup

A plastic phantom designed to approximate the proportions of the head and torso of a human subject was used for the experiments to evaluate MRI-related heating for the VNS Therapy System, as previously described (7,8,11,12). The phantom was filled to a depth of 9.5 cm (total mass, 50 kg) with a gelling agent in an aqueous solution to create a conductivity of 0.5 S/m (i.e., 0.8 g/L NaCl plus 5.85 g/L polyacrylic acid in distilled water). Because this experimental setup lacks blood flow (8,11), it simulates an extreme condition used to assess MRI-related heating for the VNS Therapy System.

A plastic frame was placed at the bottom of the phantom along with small plastic posts that were used to maintain the positions of the PG and lead in order to simulate possible in situ positions for the VNS Therapy System.

1 Configuration no. 1, the PG and lead, with the lead positioned to form a strain relief bend and a strain relief loop (i.e., this provides adequate slack and allows for neck movement by the patient) (Fig. 1), as per the manufacturer’s recommendations (6).

2 Configuration no. 2, the PG and lead, with the lead placed without strain relief, with the excess lead wrapped around the perimeter of the PG (note: although this is not in accordance with the manufacturer’s labeling, VNS Therapy Systems are sometimes implanted without adequate strain relief) (Fig. 1).

3 Configuration no. 3, no pulse generator, lead positioned to form a strain relief bend and a strain relief loop as described in configuration no. 1.

These positioning scenarios, including having the lead present without the PG, were studied because they represent diverse but clinically utilized implant configurations that may be found in patients referred for MRI examinations and were expected to yield different MRI-related heating results. Tables 1 to 3 summarize the experimental conditions used for the MRI-related heating experiments.

Temperature Recording System and Placement of Thermometry Probes

Temperature recordings were obtained using a Model 3100 Fluoroptic Thermometry System with Model SFF probes (Luxtron, Santa Clara, Calif., USA). The sensor portions of the thermometry probes were positioned to record representative sites that would generate the greatest heating for the VNS Therapy System during MRI, based on previously published literature (7,8) and pilot experiments conducted by our group (i.e., pilot experiments verified that the lead was the predominant site of heating). For experimental conditions, configuration nos. 1 and 2, the thermometry probes were positioned, as follows:

- probe no. 1, sensor portion of the thermometry probe placed in contact with the distal electrode of the lead;
- probe no. 2, sensor portion of the thermometry probe placed in contact with the proximal electrode of the lead; and
- probe no. 3, sensor portion of the thermometry probe placed in contact with the PG.

For experimental condition, configuration no. 3, the thermometry probes were positioned as follows:

- probe no. 1, sensor portion of the thermometry probe placed in contact with the distal electrode of the lead;
Table 1. Summary of MRI-Related Heating for the VNS Therapy System: 1.5 T, Transmit RF Body Coil, Whole Body Averaged SAR, 1.4 W/kg

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Configuration</th>
<th>PG</th>
<th>Lead</th>
<th>Scan site</th>
<th>Highest temp. change</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>+4.8°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>2</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>C-spine/shoulder</td>
<td>+11.5°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>3</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>L-spine</td>
<td>+0.0°C</td>
<td>Not applicable</td>
</tr>
<tr>
<td>4</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>+0.7°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>5</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>C-spine/shoulder</td>
<td>+2.0°C</td>
<td>PG</td>
</tr>
<tr>
<td>6</td>
<td>no. 3</td>
<td>None</td>
<td>302</td>
<td>Head</td>
<td>+4.4°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>7</td>
<td>no. 3</td>
<td>None</td>
<td>302</td>
<td>C-spine/shoulder</td>
<td>+9.0°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>8</td>
<td>no. 3</td>
<td>None</td>
<td>300</td>
<td>Head</td>
<td>+9.5°C</td>
<td>Proximal electrode</td>
</tr>
<tr>
<td>9</td>
<td>no. 3</td>
<td>None</td>
<td>300</td>
<td>C-spine/shoulder</td>
<td>+29.2°C</td>
<td>Proximal electrode</td>
</tr>
</tbody>
</table>

Configuration no. 1, typical placement of the PG and lead, with the lead positioned to form a strain relief bend and a strain relief loop, as per the manufacturer’s recommendations; configuration no. 2, the PG and lead placed without strain relief, with the excess lead wrapped around the perimeter of the PG; configuration no. 3, no pulse generator, lead positioned to form a strain relief bend and a strain relief loop.

Table 2. Summary of MRI-Related Heating for the VNS Therapy System: 1.5 T, Transmit/Receive RF Head Coil, Whole Body Averaged SAR, 0.1 W/kg

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Configuration</th>
<th>PG</th>
<th>Lead</th>
<th>Scan site</th>
<th>Highest temp. change</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>0.0°C</td>
<td>Not applicable</td>
</tr>
<tr>
<td>2</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>+0.2°C</td>
<td>Proximal electrode</td>
</tr>
<tr>
<td>3</td>
<td>no. 3</td>
<td>None</td>
<td>302</td>
<td>Head</td>
<td>+0.1°C</td>
<td>Lead connector</td>
</tr>
<tr>
<td>4</td>
<td>no. 3</td>
<td>None</td>
<td>300</td>
<td>Head</td>
<td>0.0°C</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Configuration no. 1, typical placement of the PG and lead, with the lead positioned to form a strain relief bend and a strain relief loop, as per the manufacturer’s recommendations; configuration no. 2, the PG and lead placed without strain relief, with the excess lead wrapped around the perimeter of the PG; configuration no. 3, no pulse generator, lead positioned to form a strain relief bend and a strain relief loop.

Table 3. Summary of MRI-Related Heating for the VNS Therapy System: 3 T, Transmit RF Body Coil, Whole Body Averaged SAR, 3 W/kg

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Configuration</th>
<th>PG</th>
<th>Lead</th>
<th>Scan site</th>
<th>Highest temp. change</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>+0.4°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>2</td>
<td>no. 1</td>
<td>102</td>
<td>302</td>
<td>C-spine/shoulder</td>
<td>+0.5°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>3</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>Head</td>
<td>+3.0°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>4</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>C-spine/shoulder</td>
<td>+14.7°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>5</td>
<td>no. 2</td>
<td>102</td>
<td>302</td>
<td>L-spine</td>
<td>0.0°C</td>
<td>Not applicable</td>
</tr>
<tr>
<td>6</td>
<td>no. 3</td>
<td>None</td>
<td>302</td>
<td>Head</td>
<td>+0.6°C</td>
<td>Lead connector</td>
</tr>
<tr>
<td>7</td>
<td>no. 3</td>
<td>None</td>
<td>300</td>
<td>Head</td>
<td>+0.4°C</td>
<td>Distal and proximal electrodes</td>
</tr>
<tr>
<td>8</td>
<td>no. 3</td>
<td>None</td>
<td>302</td>
<td>C-Spine/shoulder</td>
<td>+2.4°C</td>
<td>Distal electrode</td>
</tr>
<tr>
<td>9</td>
<td>no. 3</td>
<td>None</td>
<td>300</td>
<td>C-spine/shoulder</td>
<td>+0.9°C</td>
<td>Lead connector</td>
</tr>
</tbody>
</table>

Configuration no. 1, typical placement of the PG and lead, with the lead positioned to form a strain relief bend and a strain relief loop, as per the manufacturer’s recommendations; configuration no. 2, the PG and lead placed without strain relief, with the excess lead wrapped around the perimeter of the PG; configuration no. 3, no pulse generator, lead positioned to form a strain relief bend and a strain relief loop.
• probe no. 2, sensor portion of the thermometry probe placed in contact with the proximal electrode of the lead; and
• probe no. 3, sensor portion of the thermometry probe placed in contact with the lead connector.

The thermometry probes were visually inspected immediately before and after each MRI-heating experiment to ensure that they were properly positioned.

**MR Systems and Conditions**

MRI-related heating was studied for the VNS Therapy System using scanners operating at 1.5 and 3 T, as follows: 1.5 T/64 MHz (Signa, Excite; software version, 11.0; GE Healthcare, Milwaukee, Wis, USA) using a transmit/receive RF body coil and a transmit/receive RF head coil; 3 T/128 MHz (Signa, Excite; software version, G3.0-052B; GE Healthcare) using a transmit/receive body coil.

For the 1.5-T experiments, two different sets of MRI parameters were used to apply relatively high MR system-reported SAR levels for the scanner used in this investigation, as follows:

1. **Transmit/receive RF body coil; fast spin echo pulse sequence; axial plane; repetition time, 275 msec; echo time, 20 msec; echo train length, 8; bandwidth, 16 kHz; field of view, 40 cm; imaging matrix, 256 × 256; section thickness, 10 mm; section gap, 1 mm; number of section locations, 27; number of excitations, 4; phase direction, anterior to posterior; imaging time, 15 min.**

   The MR system reported, whole body averaged SAR was 1.4 W/kg (note: due to the software used on this scanner, the highest achievable MR system reported whole body average SAR was 1.4 W/kg).

   Because the anatomic site for the MRI procedure in relation to the position of an implanted, electronically activated device (e.g., neurostimulation system, pacemaker) impacts MRI-related heating due to exposing more or less of the implant within the transmit RF coil (7–9,11), different landmarking positions (i.e., the anatomic region for the MRI procedure) were evaluated. Thus, the landmarking positions and section locations were selected to simulate examinations involving the following anatomic regions: head (i.e., imaging the “head” portion of the phantom, 14.5 cm from the top of the phantom), cervical spine (C-spine)/shoulder (i.e., 5 cm from the top of the torso portion of the phantom with section locations selected to cover this entire anatomic region in the axial plane), and the lumbar spine (L-spine, 5 cm from the bottom of the phantom) (Table 1).

2. **Transmit/receive RF head coil; fast spin echo pulse sequence, double echo; axial plane; repetition time, 1750 msec; echo time, 20 msec, 120 msec; echo train length, 10; flip angle, 90 degrees; bandwidth, 16 kHz; field of view, 22 cm; imaging matrix, 256 × 192; section thickness, 5 mm; section gap, 1 mm; number of section locations, 48; number of excitations, 3; phase direction, anterior to posterior; imaging time, 15 min.**

   The MR system reported, whole body averaged specific absorption rate was 0.1 W/kg (note: due to the software used on this scanner, the highest achievable MR system reported whole body average SAR was 0.1 W/kg). The landmarking position and section locations were selected to simulate an examination of the head (Table 2).

For the 3-T experiments, MRI parameters were used to apply a relatively high SAR level for the scanner used in this investigation, as follows: fast spin echo pulse sequence; axial plane; repetition time, 450-msec; echo time, 14 msec; echo train length, 14; bandwidth, 16 kHz; field of view, 40 cm; imaging matrix, 256 × 192; section thickness, 10 mm; section gap, 1 mm; number of section locations, 27; number of excitations, 6; phase direction, anterior to posterior; imaging time, 15 min. The MR system reported, whole body averaged SAR was 3 W/kg. The landmarking positions and section locations were selected to simulate examinations involving the following anatomic regions: head, cervical spine (C-spine)/shoulder, and lumbar spine (L-spine) (Table 3).

**Experimental Protocol**

The VNS Therapy System was positioned on the plastic frame using the adjustable posts. The thermometry probes were positioned, as previously described. The phantom was filled with the gelled-saline solution and allowed to equilibrate.
to the environmental temperature. After recording baseline temperatures (2 min), MRI was performed for 15 min with temperatures recorded at 10-sec intervals. Post-MRI temperatures were recorded for 2 min at 10-sec intervals. This basic protocol has been utilized to assess MRI-related heating for other electronically activated devices including neurostimulation systems and pacemakers (7,8,11).

**Assessment of Function Changes for the VNS Therapy System**

For scenarios that included the pulse generator, the VNS Therapy System underwent testing of critical functional parameters according to manufacturer-derived specifications before and after exposure to the MRI conditions shown in Tables 1 to 3 to determine if these scenarios changed the function of the device. Functional testing of the VNS Therapy System was performed in a comprehensive manner by experienced professionals from Cyberonics Inc. (J.B. and D.M.I.) using appropriate instrumentation. The following functions were tested using an automated test fixture: output current, pulse-width, frequency, pulse rise time, pulse fall time, pulse overshoot, on time, off time, ramp time, lead impedance measurement function, magnet activation function, reset function, active discharge, lead to can capacitance, and serial number. The combination of direct communication with the PG and different attached external impedances was used to test these functions with results collected by observation of PG electrical output and communication responses.

**RESULTS**

**MRI-Related Heating**

The experiments performed to assess heating for the VNS Therapy System are summarized in Tables 1 to 3. At 1.5 T using the transmit RF body coil and a whole body averaged SAR of 1.4 W/kg, the temperature changes ranged from 0.0°C (configuration no. 1; PG connected; scan site, L-spine) to +29.2°C (configuration no. 3, no PG connected; scan site, C-spine/shoulder). The highest temperatures were related to the use of configuration no. 1 (comparing experiments no. 1 to no. 4), the C-spine/shoulder scan area (comparing experiments no. 2 to no. 5), and the removal of the PG (comparing experiments no. 2 to no. 9) (Table 1). With the exception of experiment no. 2, the sites of the highest temperature changes were the distal and proximal electrodes of the leads (the highest temperature for the distal lead was +1.8°C in this case). Figure 2 shows the highest temperature change measured at 1.5 T (experiment no. 9).

![Figure 2](image-url)

_Figure 2._ MRI-related heating for the VNS Therapy System: 1.5 T using the transmit RF body coil and an MR system reported whole body averaged SAR of 1.4 W/kg, experiment no. 9 (configuration no. 3, no PG connected; scan site, C-spine/shoulder). The site of the highest temperature change was the proximal electrode, 29.2°C (probe 1, distal electrode; probe 2, proximal electrode; probe 3, lead connector).
At 1.5 T using the transmit/receive RF head coil and a whole body averaged SAR of 0.1 W/kg, the temperature changes ranged from 0.0°C to +0.2°C, indicating that minimal temperature alterations occurred using these MRI conditions (Table 2).

At 3 T using the transmit RF body coil and a whole body averaged SAR of 3 W/kg, the temperature changes ranged from 0.0°C (configuration no. 2; PG connected; scan site, L-spine) to +14.7°C (configuration no. 2; PG connected; scan site, C-spine/shoulder). The highest temperatures were related to the use of configuration no. 2 (comparing experiments no. 1 to no. 3 and no. 2 to no. 4), the C-spine/shoulder scan area (comparing experiments no. 2 to no. 4), and the removal of the PG (comparing experiments no. 1 to no. 6 and no. 2 to no. 8) (Table 3). The sites of the highest temperature changes were the distal and proximal electrodes of the leads.

### Functional Changes

Tests conducted to assess the function of the VNS Therapy System indicated that MRI performed using various conditions at 1.5 T and 3 T produced no significant alterations in the operation of this device.

### DISCUSSION

Theoretical and realistic risks posed by the use of MRI in a patient with a neurostimulation system include those associated with magnetic field interactions, MRI-related heating, induced currents, and alteration or damage to the operational aspects of the device (3,7,8,10). Based on findings from MRI evaluations performed using a variety of conditions to study different types of neurostimulation systems, magnetic field interactions, induced currents, and changes in function do not appear to be problematic for these devices (3,7,8,13,14). The predominant concern for neurostimulation systems is MRI-related heating, which can be excessive under certain circumstances (3,7–10,13), while others are less problematic. Data obtained from comprehensive testing of neurostimulation systems has resulted in FDA-approved labeling claims that indicate specific guidelines that must be followed to ensure patient safety (3,6,10). Reports of patients with neurostimulation systems experiencing significant adverse effects in association with MRI-related heating stress the critical importance of following these recommendations (9,10). To date, with careful adherence to safety recommendations issued by device manufacturers, there has been no serious injury or incident reported for a patient with a neurostimulation systems undergoing MRI (9,10).

The static magnetic field of the MR system can exert translational attraction and torque on the PG and lead of the VNS Therapy System, resulting in possible displacement of these components. However, the Model 102 PG assessed in this study has fewer and smaller ferromagnetic parts than the Model 100 PG, which was previously reported by Benbadis et al. (3) to exhibit magnetic qualities that were relatively minor in association with exposure to a 1.5-T scanner. At 3 T, the Model 102 showed a deflection angle of only 34 degrees when placed at the point of the highest spatial gradient of a 3-T MR system (January 2006; unpublished observations, Jason Begnaud, data on file. Cyberonics, Inc.). If an implant deflects less than 45 degrees, then the magnetically induced deflection force is less than the force on the implant due to gravity (11). As such, there is no risk of movement or dislodgement of the Model 102 PG in a 3-T environment. Furthermore, once implanted, substantial retentive forces are provided by sutures or other means of fixation, including those associated with tissue granulation (which develops within a few weeks after implantation) that create counter-forces, effectively preventing the PG from presenting a safety issue in a patient undergoing MRI at 3 T. The Model 300 and Model 302 leads are made from platinum-iridium and MP35N, which are materials known to have low magnetic susceptibilities. Therefore, there is no static magnetic field-related problem for the leads used for this device.

### MRI-Related Heating

Radiofrequency fields used during MRI generate currents in electrical conductors, resulting in induced voltages and heating that is greatest where the electrical current flux density is highest. For neurostimulation systems and pacemakers, the predominant site of heating is at the electrode (3,8,10,11,15,16). Thus, the most compelling and problematic safety issue for neurostimulation
systems is that of MRI-related heating of the electrodes. For a neurostimulation system, MRI-related heating is impacted by intrinsic as well as extrinsic factors (9,10). The configuration of the positioning of the system (lead and PG) and the length and routing of the lead will produce heating variances (11). Extrinsic factors such as the field strength of the MR system, the type of transmit RF coil used (e.g., body, head, or extremity), the landmarking or anatomic site undergoing the scan (i.e., relative to the position of the neurostimulation system), the amount of RF energy used for imaging (i.e., the whole body averaged SAR), and how the SAR is calculated by a given MR system also create differences in heating effects (11,16).

Not surprisingly, data acquired using *in vitro* techniques indicated that substantial heating occurs for certain conditions, while others produce relatively minor, physiologically inconsequential temperature alterations for the neurostimulation systems (3,7,8,13). In consideration of the myriad of variables known to affect MRI-related heating for these devices and to evaluate the possible expansion of safety guidelines for MRI, the VNS Therapy System in this investigation was evaluated at 1.5 and 3 T using various device configurations and MRI conditions.

Using the transmit RF body coil at 1.5 and 3 T, findings from the MRI-related heating experiments indicated that the highest temperature changes for the VNS Therapy System tended to occur with the landmark position that involved the lead (i.e., C-spine/shoulder area), while the lowest temperature changes occurred for the landmark position far removed from this device (i.e., L-spine). MRI-related heating varied when selecting the head landmark position and depended on the field strength/frequency used for MRI, the configuration of the VNS Therapy System, and whether or not the PG was connected to the lead. For example, at 1.5 T, configuration no. 2 (lead placed without strain relief, with the excess lead wrapped around the perimeter of the PG) generated a substantially lower temperature change compared to configuration no. 1 (lead positioned to form a strain relief bend and a strain relief loop). Furthermore, removing the PG caused moderate-to-high temperature changes.

By comparison, at 3 T, both configurations produced acceptable temperature increases (i.e., ≤±3°C; note: RF thermal ablation techniques have been shown to cause reversible lesions when the local temperature is elevated to a range of 42-44°C, while irreversible lesions occur at temperatures that exceed 45°C (17). Therefore, a transient temperature elevation of 3°C or less is unlikely to cause significant adverse thermogenic-related effects.). Removing the PG did not greatly impact the temperature alterations (temperature changes ≤+0.6°C).

It should be noted that, at 3 T, the “no strain relief” configuration (configuration no. 2) caused a +3.0°C temperature increase when using the transmit body RF coil, while the “strain relief” configuration (configuration no. 1) caused only a +0.4°C temperature elevation. Interestingly, configuration no. 1 caused a +4.8°C temperature increase when using the 1.5-T MR system and the transmit body RF coil while configuration no. 2 caused only a +0.7°C temperature increase. As such, patients should not be scanned utilizing the MRI conditions described here in association with the positioning scenarios that cause temperature increases greater than +3.0°C.

At 1.5 T, using the transmit/receive RF head coil at a whole body averaged SAR of 0.1 W/kg, MRI-related heating was ≤+0.2°C for all of the conditions studied. This is not surprising in consideration of the fact that the RF energy was confined to an area that did not involve the lead of the VNS Therapy System. Similar findings have been reported for experiments involving a cardiac pacemakers (11). While we did not examine MRI-related heating for the use of a transmit/receive RF head coil at 3 T, we anticipate that similar results will occur; however, this remains to be verified by additional investigation.

To prevent substantial MRI-related heating of the VNS Therapy System, a conservative approach to scanning patients at 1.5 and 3 T may be implemented by confining the examinations to specific transmit RF coil configurations, body parts removed from this device (e.g., lumbar spine and lower extremities), and/or decreasing the amount of RF power used (i.e., whole body averaged SAR) for the procedure. A similar strategy has been used to prevent MRI-induced lead heating for neurostimulation systems and cardiac pacemakers (7,8,10,11). As previously indicated, MRI-related heating of implants tends to be substantially less when using a transmit head or transmit extremity coil.
compared to a transmit body coil because the overall area subjected to RF energy is minimized and the SAR level for a given pulse sequence in inherently less (7, 10, 11).

**Function**

Exposure to the electromagnetic fields used for MRI may result in malfunction of, or damage to, the pulse generator of a neurostimulation system. Findings from comprehensive testing conducted to evaluate the functional aspects of the VNS Therapy System indicated that MRI procedures performed using various exposure conditions at 1.5-T and 3-T produced no significant alterations in the operation of the pulse generators involved in this study and under the MRI conditions that were used.

**Safety Recommendations for the VNS Therapy System**

Based on the results of the tests performed in this investigation, and in consideration of the current manufacturer's labeling (6), conservative guidelines (those that do not cause an increase in temperature of $\geq \pm 3.0^\circ$C) have been developed for scanning patients using 1.5- and 3-T MR systems to ensure safety. Notably, these recommendations apply to adult-sized patients only.

1. The MRI procedure should not be performed if the patient is unable to communicate with the MR system operator (e.g., due to language barrier, altered mental status, sedation).
2. Provide the patient with a means to alert the MR system operator of any unusual sensations or problems.
3. The MRI examination must be supervised and set up by an MRI-trained radiologist, MRI physicist, or MRI technologist with knowledge about how to achieve proper MR system reported SAR levels and utilize them for the examination.
4. At 1.5 and 3 T, MRI should not be performed on or near the cervical spine, shoulder, or any area in proximity of the lead and pulse generator of the VNS Therapy System.
5. At 1.5 T, MRI of the brain/head may be performed using a transmit/receive RF head coil at a whole body averaged SAR of $\leq 0.1$ W/kg.
6. At 1.5 T, MRI of the L-spine and lower extremities may be performed using a transmit RF body coil, and receive-only local coil or transmit/receive extremity coil at an MR system reported whole body averaged SAR of $\leq 1.4$ W/kg.
7. At 3 T, MRI of the L-spine and lower extremities may be performed using a transmit RF body coil, and receive-only local coil or transmit/receive extremity coil at an MR system reported whole body averaged SAR of $\leq 3$ W/kg.
8. Instruct patient to notify MR system operator of pain, discomfort, heating, or other unusual sensation so that the operator can immediately terminate the procedure, as needed.
9. Maintain visual and voice contact throughout the procedure with the patient.
10. Prior to being allowed into the MRI environment, the patient with the VNS Therapy System must have the device programmed by an appropriate healthcare professional using the VNS Therapy Programming System. The PG must be programmed to a normal mode output current of 0 mA and the magnet mode output current to 0 mA.
11. Following the MRI procedure, an appropriate healthcare professional should use the VNS Therapy Programming System to assess the condition of the VNS Therapy System. If the device 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 prior to the MRI procedure. Assessment of the system diagnostics should indicate “Impedance = OK.”

**SUMMARY AND CONCLUSIONS**

The VNS Therapy System was studied using *in vitro* techniques to assess MRI-related heating at 1.5 and 3 T using different leads, positioning configurations, transmit RF coils (body and head), levels of RF power (SAR), and scans on different body regions. This investigation identified potentially unsafe as well as safe conditions with regard to MRI-related heating. Device function was unaffected by MRI procedures performed at 1.5 and 3 T. By following specific conditions, the safety guidelines for the VNS Therapy System can be expanded beyond those currently recommended by the manufacturer.
Similar to MRI safety guidelines for other electronically activated implants (16), the information presented herein is specific to the VNS Therapy System (PG and two different leads) that was evaluated, the configurations studied, and the MRI conditions associated with the use of 1.5- and 3-T MR systems. The exact safety criteria for the particular neurostimulation system with regard to the pulse generator, lead, operational conditions for the device, the positioning of the components, and the MR system conditions must be carefully followed for MRI. Different device or MRI conditions may alter the safety profile for the VNS Therapy System.

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