LETTERS TO THE EDITOR

Response to Shellock et al. “Vagus Nerve Stimulation Therapy System: In Vitro Evaluation of Magnetic Resonance Imaging-Related Heating and Function at 1.5 and 3 Tesla”

To the Editor:

The article “Vagus Nerve Stimulation Therapy System: In Vitro Evaluation of Magnetic Resonance Imaging-Related Heating and Function at 1.5 and 3 Tesla” by Shellock et al. provides safety recommendations for magnetic resonance (MR) scanning procedures in 1.5 and 3 tesla (T) MR systems, which extend beyond those currently labeled by the manufacturer and approved by the Food and Drug Administration (FDA). FDA has several concerns with the conclusions drawn in this article based on the limited testing. Some of these concerns are:

1. The safety recommendations are based on force, torque, and heating measurements and functional evaluation of the vagus nerve stimulation (VNS) therapy system after the MR scanning procedure. However, other effects such as nerve stimulation and nerve damage due to induced currents from the gradient fields or device monitoring during the scanning are not included in the testing.

2. Only three implant configurations were used and worst case positioning of the VNS therapy system was not evaluated, although heating up to 29.2°C was found for a certain landmark and configuration. It is unknown whether other implant configurations in other MR systems would result in heating up to similarly dangerous temperatures even in the “safe” recommended landmark position.

3. The conclusions drawn in this article are based on the MR system reported whole body averaged specific absorption rate (SAR) for a phantom. Although the whole body averaged SAR reported by MR systems is relevant to patients, it is well-known that the SAR reported by MR systems is not accurate for phantoms and should therefore not be used for heating evaluations of implants.

4. The safety recommendations provided in this article generally refer to 1.5 and 3 T MR systems, although testing was done with only one 1.5- and one 3-T MR system. However, it is well-known that different MR systems may have completely different effects on implants in terms of displayed vs. actual SAR, heating, induced currents, etc. Therefore, we would consider the results from this study to apply only to heating effects in the phantom for the three specified VNS therapy system configurations and only for the two specific MR systems tested.
In conclusion, FDA is concerned that the generalizations and extrapolations to MR systems, implant configurations, and actual VNS patients, in the variety of MR scanners and system configurations, using this limited-scope phantom testing could have serious adverse health consequences for the patient. While we strongly support the concept of more rigorous bench, animal, and clinical testing to explore the expansion of current MR safety recommendations for VNS patients, in the absence of such testing we continue to recommend adherence to the current FDA-approved labeling.

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LETTERS TO THE EDITOR

Response to Kainz

To the Editor:

In a Letter to the Editor dated August 23, 2006, Dr. Kainz of the U.S. Food and Drug Administration, Center for Devices and Radiological Health, comments on the article I coauthored titled “Vagus Nerve Stimulation Therapy System: In Vitro Evaluation of Magnetic Resonance Imaging-Related Heating and Function at 1.5 and 3 Tesla.” In his comments, Dr. Kainz raises several concerns with the article, its conclusions, and what Dr. Kainz characterizes as the study’s “limited testing.” The authors welcome the opportunity to elaborate on the article and this important issue by responding to Dr. Kainz’s points.

1. Dr. Kainz raises concerns that induced currents from gradient fields should be considered when evaluating the safety of active implantable medical devices with magnetic resonance (MR) systems. Although evaluation of induced currents with active medical devices is a consideration, this aspect of MRI safety testing was not within the scope of this particular evaluation. Additional analysis of induced currents from gradient fields has already been performed in other studies (data on file, Cyberonics Inc., Houston, TX, USA), and that analysis demonstrates that the potential for induced current injuries is negligible in VNS Therapy System patients being scanned in ISO 60601-2-33-2nd Edition-compliant MR systems operating at the Normal or First Level Controlled Modes.

2. With regard to Dr. Kainz’s concerns regarding the evaluation of MRI-related heating, the study utilized the American Society for Testing and Measurement (ASTM International) F2182-02a, Standard Test Method for Measurement of Radio Frequency Induced Heating Near Passive Implants During Magnetic Resonance Imaging. Dr. Kainz points out that “only three implant configurations were used and worst case positioning of the VNS Therapy System was not evaluated . . .” and other positioning in other MR systems could result in unsafe heating scenarios. Because the VNS Therapy stimulating electrodes must be implanted in the cervical area of the left vagus nerve, there are a limited number of implant configurations, which are clinically relevant. Importantly, the lead configurations discussed in the article reflect both the realistic worst case and relevant clinical scenarios as indicated by ASTM F2182-02a, while remaining consistent with labeling and
known implant geometry used by surgeons to implant the VNS Therapy System.

3. Dr. Kainz expresses concern regarding the accuracy of the reported whole body averaged specific absorption rate (SAR) by MR systems and the use of phantoms to demonstrate safety. ASTM F2182-02a specifies use of an adult-sized phantom and to “record the applied whole body averaged SAR reported by the MR system software.” In reality, there is currently no consensus on this matter among the MRI safety testing community, the ASTM, the MR system manufacturers, or experts in the field as to the use of SAR and phantoms, or the appropriate test methods to use to study MRI-related heating.

4. Dr. Kainz correctly points out that testing reported in this article was done with only one 1.5-T and one 3-T MR scanner. As discussed in the article, “[s]imilar to MRI safety guidelines for other electronically activated implants, 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.” Given this, the results reported in the article should only apply to the MR scanners and VNS Therapy Systems tested. Data should not be extrapolated to include scanners and coils, which have not been tested.

Finally, the article was made available in this forum for clinicians, researchers, and other medical device manufacturers to share the experience and knowledge base in regards to the use of MRI and this active medical device implant. Although this report outlines the conclusions drawn from the in vitro evaluation of MRI related heating and function in relation to 1.5 and 3 Tesla GE Signa Excite systems, the article was not meant to suggest the use of MRI outside of the approved labeling. Dr. Kainz’s thorough review of the article is appreciated. He highlights some very interesting points that are a concern for the medical device industry in the evaluation of MR safety. Although the authors are confident that the data presented represent a thorough evaluation of the performance of the VNS Therapy System on two different MR systems, physicians and MRI technicians should adhere to current approved labeling.

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LETTERS TO THE EDITOR

Response to Shellock

To the Editor:

Thank you for a copy of Dr. Shellock’s response and the opportunity to reply. Dr. Shellock raises several important points in his response. However, I am not in agreement with many of his conclusions and some of my concerns were not addressed satisfactorily by Dr. Shellock’s response.

1. Induced currents from gradient fields: Dr. Shellock mentions an additional study; however, no data or details regarding that study are given. Therefore, I cannot comment on the quality and applicability of this study and the appropriateness of the measurement apparatus used for assessing the induced currents.

2. Electromagnetic compatibility (EMC) testing: Magnetic resonance imaging (MRI)–induced electromagnetic interference (EMI) has the potential to alter the device functions, even for devices that are deactivated. Therefore, I continue to believe that pre- and post-MR scan evaluations alone are not sufficient to show EMC MRI compatibility.

3. Implant configuration and worst case condition: It is very important to realize that the scope of ASTM F2182-02a covers only passive implants. Although it may be possible to adjust F2182-02a for active implants, it is not clear that appropriate adjustment methods were incorporated in this study. While I agree that there are a limited number of clinically relevant implant configurations for a patient, I continue to believe that worst case conditions should be established in the phantom, and these phantom worst case conditions should then be related to the exposure inside the patient. Because the field distribution inside the ASTM F2182 phantom is likely to be significantly different from the field distribution inside a patient, it is not necessarily appropriate to use the same implant configuration for the patient and the phantom. Therefore, based on the data provided from placing the implant in a physiological position in the ASTM F2182 phantom, it is not clear how the heating measured in the phantom relates to possible heating in a patient. Furthermore, the article does not provide uncertainty data, which could drastically alter the conclusions of the study.

4. System reported specific absorption rate (SAR): I disagree with Dr. Shellock’s contention that there is currently no consensus among the MRI safety testing community, the ASTM, the MR system manufacturers, experts in the field, and the Food and Drug Administration (FDA) on the usability of system reported SAR. The scientific community is well-aware of the many limitations associated with the use of system reported SAR for heating evaluations. FDA requested that the ASTM MR task force address these concerns. This task force initiated an MRI SAR Intercomparison study to compare the actual phantom SAR, using calorimetry, to the
machine reported SAR. Dr. Shellock, as a participant in the development of the protocol for the SAR Intercomparison, is aware of this project. Initial results for the MRI SAR Intercomparison show a phantom SAR underestimation by the MR system of up to seven times, which could lead to a heating underestimation by that same factor. Based on these data as well as other sources in the literature, I believe that system reported SAR is an inappropriate measure for heating evaluations of active and passive implants.

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