Vagus nerve stimulation after lead revision

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Object. Vagus nerve stimulation (VNS) has demonstrated benefit in patients with medically intractable partial epilepsy. As in other therapies with mechanical devices, hardware failure occurs, most notably within the VNS lead, requiring replacement. However, the spiral-designed lead electrodes wrapped around the vagus nerve are often encased in dense scar tissue hampering dissection and removal. The objective in this study was to characterize VNS lead failure and lead revision surgery and to examine VNS efficacy after placement of a new electrode on the previously used segment of vagus nerve.

Methods. The authors reviewed all VNS lead revisions performed between October 2001 and August 2011 at the University of Iowa Hospitals and Clinics. Twenty-four patients underwent 25 lead revisions. In all cases, the helical electrodes were removed, and a new lead was placed on the previously used segment of vagus nerve. All inpatient and outpatient records of the 25 lead revisions were retrospectively reviewed.

Results. Four cases were second lead revisions, and 21 cases were first lead revisions. The average time to any revision was 5 years (range 1.8–11.1 years), with essentially no difference between a first and second lead revision. The most common reason for a revision was intrinsic lead failure resulting in high impedance (64%), and the most common symptom was increased seizure frequency (72%). The average duration of surgery for the initial implantation in the 15 patients whose VNS system was initially implanted at the authors’ institute was much shorter (94 minutes) than the average duration of lead revision surgery (173 minutes). However, there was a significant trend toward shorter surgical times as more revision surgeries were performed. Sixteen of the 25 cases of lead revision were followed up for more than 3 months. In 15 of these 16 cases, the revision was as effective as the previous VNS lead. In most of these cases, both the severity and frequency of seizures were decreased to levels similar to those following the previous implantation procedure. Only 1 complication occurred, and there were no postoperative infections.

Conclusions. Lead revision surgery involving the placement of a new electrode at the previously used segment of vagus nerve is effective at decreasing the seizure burden to an extent similar to that obtained following the initial VNS implantation. Even with multiple lead revisions, patients can obtain VNS efficacy similar to that following the initial lead implantation. There is a learning curve with revision surgery, and overall the duration of surgery is longer than for the initial implantation. Note, however, that complications and infection are rare.

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Key Words: • epilepsy • seizure • vagus nerve stimulation • neuromodulation • vagus nerve

Vagus nerve stimulation is a useful adjunct to the armamentarium of surgical options for the treatment of epilepsy.9,10,11,14 Studies in the 1990s demonstrated a mean 25%–30% decrease in seizure frequency in epilepsy patients following VNS, which led to US FDA approval in 1997 for the treatment of intractable partial epilepsy in patients older than 12 years of age.9,21 To date, many more retrospective and nonrandomized studies have confirmed the effectiveness of VNS in children7 and adults afflicted with treatment-resistant epilepsy.5,6 Further therapeutic uses for VNS are currently being investigated and include early but encouraging results for depression13 and heart failure.18 Although peripheral nerve stimulation to treat seizures is not a new concept, the exact mechanism through which VNS decreases the seizure burden is not completely understood.22

As with most mechanical devices, hardware failure can occur in VNS for various reasons.20 Failure or depletion of the IPG or failure of the VNS lead can result in improper device function and ineffective seizure control.20 Replacing the IPG typically yields expected device function, even with multiple IPG replacements, and complications are uncommon. Lead revision can be more challenging, however (Fig. 1). The spiral-designed lead electrodes wrapped around the vagus nerve are often encased in dense scar tissue hampering dissection and removal (Fig.
The etiology of lead failure, time to failure, and complication rate of lead revision have not been fully elucidated. Furthermore, VNS efficacy is unclear after placement of a new electrode on the previously used segment of vagus nerve encased in scar tissue (Fig. 1C). There are relatively few studies that characterize VNS lead revision and discuss VNS efficacy in seizure reduction following a revision as compared with effectiveness following the initial lead implantation.

**Methods**

**Patient Population**

After the University of Iowa Institutional Review Board approved the study, all VNS lead implantations were identified through a neuromodulation patient registry. Two hundred twenty-three VNS lead implantations were performed between October 2001 and August 2011 at the UIHC. One hundred ninety-eight patients underwent initial VNS implantations, and 24 underwent 25 VNS lead revisions. Among these 25 revision cases, the previous VNS lead had been implanted at UIHC in 15 cases and at another institution in 10.

All patients were treated by a single neurosurgeon (H.K.). All inpatient and outpatient records were retrospectively reviewed, and the following data were recorded: patient age, sex, age at lead implantation or revision, date of last follow-up, seizure modality, frequency of seizures before and after initial lead implantation and before and after lead revision, lead failure symptoms, lead impedance at revision, lead fracture, history of VNS system–related infection, recent head or neck trauma, surgical findings, use of microscope, and postrevision complications and infection.

Prior to VNS implantation, all patients underwent evaluation at a multidisciplinary epilepsy surgery conference and were recommended for surgery. A multidisciplinary approach was also conducted for VNS lead revision, and the decision to perform a revision was based on lead impedance, integrity of the lead and IPG, patient symptoms, and seizure frequency. Vagus nerve stimulation therapy in patients with generalized epilepsy and in children younger than the age of 12 years is an off-label use and is not approved by the FDA.

**Surgical Technique: Initial Implants**

Initial implantations in all patients were performed using standard VNS techniques. In brief, all VNS leads (Cyberonics, Inc.) were placed on the left vagus nerve while patients were under general anesthesia. A left-sided transverse neck incision from the sternocleidomastoid to the midline was made for neck dissection and vagus nerve exposure for lead implantation. An infracavicular chest incision was performed for IPG placement, and leads were tunneled subcutaneously from the neck to the chest incision. In each patient the lead and IPG were implanted in a single operation. Prophylactic perioperative antibiotics—nafcillin or vancomycin if the patient was allergic to penicillin—were used for all implantation surgeries, beginning at least 30 minutes prior to incision and continuing for 24 hours postoperatively.

**Surgical Technique: Revisions**

In brief, revision surgery was performed through the previous surgical incision on the left without increasing the length of the incision. A sharp left-sided neck dissection was performed to access the VNS helical lead electrodes (Fig. 1A). The old VNS lead was removed (Fig. 1B), and a new lead was placed on the segment of vagus nerve used by the previous electrode (Fig. 1C). In nearly all cases, the IPG was replaced at the infracavicular pocket at the time of lead revision. In the first 9 lead revisions, the microscope was used for dissection of the old lead from the vagus nerve. Magnification with loupes was used in the last 16 revisions. All other aspects of lead revision were similar to the initial implantation.

**Results**

**Patient Demographics and Characteristics**

Twenty-four patients underwent 25 VNS revisions between October 2001 and August 2011 at UIHC (Table 1). Of these 25 revisions, 4 were second and 21 were first lead revisions. There were 15 male (62.5%) and 9 female (37.5%) patients, of whom 23 were adults (96%). The most common type of epilepsy was partial, with 22 (92%) of 24 patients having some form of partial epilepsy. The mean patient age at the previous implantation was 32 years.
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TABLE 1: Summary of data in 25 cases of VNS lead revision*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Revision No.</th>
<th>Time to Revision (yrs)</th>
<th>Impedance</th>
<th>Lead Fracture</th>
<th>History of VNS Infection</th>
<th>Lead Failure Symptoms</th>
<th>Sz Frequency After Revision†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>1st</td>
<td>3.8</td>
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<td>no</td>
<td>increased Szs</td>
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</tr>
<tr>
<td>2</td>
<td>M</td>
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<td>3.7</td>
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<td>increased Szs</td>
<td>unknown</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>1st</td>
<td>7.4</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>none</td>
<td>decreased</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>1st</td>
<td>1.8</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>none</td>
<td>decreased</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>2nd</td>
<td>3.3</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>none</td>
<td>decreased</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>1st</td>
<td>3.4</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>increased Szs</td>
<td>unknown</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>1st</td>
<td>11.1</td>
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<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
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<td>M</td>
<td>1st</td>
<td>3.4</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>increased Szs &amp; shock sensation</td>
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<td>9</td>
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<td>high</td>
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<td>no</td>
<td>none</td>
<td>decreased</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>1st</td>
<td>7.0</td>
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<td>no</td>
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</tr>
<tr>
<td>12</td>
<td>M</td>
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<td>6.0</td>
<td>NA</td>
<td>no</td>
<td>yes</td>
<td>NA</td>
<td>unknown</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>1st</td>
<td>6.3</td>
<td>normal</td>
<td>yes</td>
<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>1st</td>
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<td>unknown</td>
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<td>1st</td>
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<td>no</td>
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<td>decreased</td>
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<td>16</td>
<td>M</td>
<td>1st</td>
<td>8.4</td>
<td>short circuit</td>
<td>no</td>
<td>no</td>
<td>increased Szs</td>
<td>unknown</td>
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<tr>
<td>17†‡</td>
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<td>5.4</td>
<td>high</td>
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<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
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<td>F</td>
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<td>5.3</td>
<td>high</td>
<td>no</td>
<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>1st</td>
<td>2.3</td>
<td>normal</td>
<td>no</td>
<td>no</td>
<td>increased Szs &amp; shock sensation</td>
<td>decreased</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>1st</td>
<td>3.4</td>
<td>high</td>
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<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
<tr>
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<td>M</td>
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<td>no</td>
<td>increased Szs</td>
<td>decreased</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>2nd</td>
<td>4.2</td>
<td>normal</td>
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<td>yes</td>
<td>increased Szs &amp; neck/chest pain</td>
<td>unknown</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>1st</td>
<td>5.6</td>
<td>short circuit</td>
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<td>no</td>
<td>increased Szs &amp; paresthesias</td>
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</tr>
<tr>
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<td>M</td>
<td>2nd</td>
<td>8.0</td>
<td>high</td>
<td>no</td>
<td>yes</td>
<td>none</td>
<td>unknown</td>
</tr>
<tr>
<td>25</td>
<td>M</td>
<td>1st</td>
<td>4.3</td>
<td>normal</td>
<td>yes</td>
<td>no</td>
<td>none</td>
<td>decreased</td>
</tr>
</tbody>
</table>

* NA = not applicable; Sz = seizure.
† As compared with prior to surgery and before initial VNS implantation.
‡ Patient with postoperative cable bowstring complication requiring revision 1 month later.

(range 4–55 years), and the mean age at lead revision was 37 years (range 8–59 years). The mean age of patients with first lead revisions was 35 years (range 8–59 years), and those with second lead revisions, 46 years (range 26–59 years). The average time to any lead revision was 5 years (range 1.8–11.1 years), with essentially no difference between a first and second lead revision. The average time to a first lead revision was 5.1 years and that to a second lead revision was 4.8 years. Time to lead revision for each type of lead failure is presented in Table 2.

Lead Impedance

Interrogation of the VNS system and determining lead impedance allow one to assess the integrity and function of the system. The deviation of impedance from normal may indicate improper device function. The patients in 18 cases (72%) presented with high impedance at the time of revision, 2 cases (8%) involved a short circuit within the system, 4 cases (16%) demonstrated normal impedance, and 1 case (4%) had no implanted VNS system and therefore no impedance reading since the system had been previously removed at another institution because of infection.

Lead Failure Etiology

The determination of lead failure (Table 2) relies on a patient’s clinical symptoms, seizure frequency, and interrogation of the system and lead impedance. Sixteen (64%) of the 18 cases with high impedance at the time of revision had no visible damage or fracture within the lead and/or cable, suggesting an intrinsic lesion within the lead and/or cable. Other causes of lead failure included visible fractures of the lead in 3 cases (12%), increasing seizure frequency and an impedance indicating a short circuit in 2 cases (8%), normal impedance but pain and shock-like sensations suspect for device malfunction in 2 cases (8%), electrode coil dislocation from the vagus nerve in 1 case (4%), and a previous hardware infection and VNS system removal in 1 case (4%).

Lead Failure Symptoms

Symptoms vary depending on the etiology of lead
failure (Table 1). The patients in 18 cases (72%) presented with increased seizure frequency; in 4 cases (16%), with neck and/or chest pain, paresthesias, or shock-like sensations—all probably the result of a short circuit within the system; and in 6 cases (24%), with no new symptoms. Additionally, 3 cases (12%) had a history of VNS-related infection, and 3 cases (12%) had a recent history of head and/or neck trauma.

**Lead Revision Surgery**

The average duration of surgery for the initial implantation in 15 patients whose VNS system was implanted at our institution was 94 minutes (range 53–195 minutes) and occurred between January 2002 and March 2008 (Fig. 2). The average duration of lead revision surgery was 173 minutes (range 108–273 minutes) and occurred between October 2005 and July 2011. The duration of the revision surgery decreased as the experience of the surgeon increased over time. In all cases, the vagus nerve was found encased in fibrous scar tissue (Fig. 1A and B). In the first 9 revision cases (between October 2005 and March 2009), a surgical microscope was used to dissect the VNS lead free from the nerve. In the last 16 revision cases (between April 2009 and July 2011), only loupe magnification and headlight illumination were used. In all cases, sharp dissection was performed. There were no postoperative infections. Only 1 patient experienced a complication requiring additional surgery; in this patient the lead cable was taut, creating a pulling sensation on neck turning.

**Seizures Before and After VNS System Implantation and Lead Revision**

Sixteen of the 25 cases of VNS lead revision were followed up for longer than 3 months at our institution to fully assess the efficacy of seizure treatment. In 15 (94%) of these 16 cases, the revision was as effective as the previous VNS system. In almost all cases, both the severity and frequency of seizures were decreased to levels similar to those following implantation of the initial VNS lead. Of the 4 second lead revisions, only 1 was followed up for longer than 3 months; this patient was found to have seizure control similar to that obtained after both the previous and the initial VNS implantation. The average follow-up in these patients was 21 months (range 3–55 months).

**Discussion**

Vagus nerve stimulation is an effective and generally safe treatment option for patients with medically intractable epilepsy.3 Randomized controlled studies in the 1990s demonstrated a 25%–30% decrease in seizure frequency, which led to FDA approval of VNS for partial epilepsy.4,9,21 Since its approval, VNS implantations have been widely performed.8 Given the increasing use of VNS for the treatment of medically intractable epilepsy, however, VNS lead failure is more commonly observed.1,8,12,15–17,19,20 The determination of lead failure relies on multiple factors, including the patient’s clinical symptoms, seizure frequency, and interrogation of the system and lead impedance. We found that lead failure occurs for a variety of reasons and in our series was most commonly observed in cases of high impedance within the VNS lead, which was found in 72% of our lead revisions (Table 1). The majority of patients (89%) who presented with high impedance had no visible damage or gross fracture of the lead or cable. The etiology of high impedance and lead failure is not entirely clear in these cases. Some have ascribed lead failure in the absence of a visible fracture...
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to “microlesions” within the lead cable, whereas others have observed lead failure without visible fractures in which they believed that significant vagus nerve scar tissue resulted in high impedance. However, we found that the placement of a new VNS lead at the previously used segment of vagus nerve provided a proper contact in all 16 such cases as well as normal impedance, implying that the presence of dense scar tissue was probably not the cause of lead failure.

In addition to an intrinsic increase in lead impedance and device failure, we observed other factors resulting in lead failure. We have found and others have observed, albeit a rare event, visible fractures within the lead cable resulting in physical disconnection and lead failure. Additionally, dislocated leads, hardware-related infection, device malfunction, and short circuits within the system were noted. Imaging of the neck and chest with radiography can often be used to diagnose visible fractures and dislocated lead coils. It is unclear at this time if there are any risk factors that may predispose someone to a specific type of lead failure. An attempt was made to correlate any recent head or neck trauma with lead failure, but in our series trauma was an uncommon occurrence.

In our study, VNS lead failure most commonly resulted in an increased seizure frequency. In some cases, a very dramatic increase in seizure intensity and frequency was observed. However, other symptoms alerted patients to device malfunction and included neck and chest pain, shock-like sensations, and paresthesia. Short circuits within the system may cause these types of symptoms. The stimulator should be turned off immediately if this occurs and interrogated. As in our series, other studies have shown that these shock-like sensations, pain, and paresthesias will resolve after revision.

We used time from previous lead implantation to lead revision to approximate the time to lead failure (Table 2). Determining the exact point of malfunction or failure isn’t always possible because VNS may have some efficacy even after device malfunction. Overall, it appears that the variation in the length of time to VNS lead failure is notable and that the average time to failure (5 years) is comparable to that in other smaller studies. This average time to failure was mostly influenced by and most representative of intrinsic lead failures, as they constituted the majority of our cases.

Vagus nerve stimulation lead revision can be challenging. As surgeon experience with lead revisions increases, the operative time decreases significantly. In our study, however, given the presence of scar tissue, it remains a longer operation than the initial implantation. Initially, the use of an intraoperative microscope probably contributed to longer surgical times. Although the normal anatomy was obscured and altered by scar tissue in all cases, we had only 1 complication after lead revision. Other authors have noted complications after lead revision including transient vocal cord paralysis. There were no infections postoperatively and therefore no increase in the postoperative infection rate as compared with historical averages.

To more efficiently, safely, and effectively revise the VNS lead, others have provided a discussion of surgical techniques. Some have advocated the use of sharp dissection, whereas others have endorsed sharp monopolar cautery to aid dissection in which dense fibrous tissue is encountered. Still others have attempted to access a naive segment of the nerve. Given the dense scar tissue, some surgeons cut the distal lead and leave the helical leads in place while a naive segment of the vagus nerve is dissected for placement of the new lead. To avoid the fibrous scar tissue, O’Neill and Wilberger described a posterior cervical triangle approach to a naive segment of the vagus nerve. In both the initial implantation and the lead revision, we used sharp dissection through the previous surgical incisions. Additionally, in an attempt to decrease scar tissue formation around the vagus nerve, we routinely cut the strings off of the helical loops of the VNS lead on implantation (Fig. 1C). We cannot yet comment on whether this strategy is effective in decreasing scar tissue formation.

We observed that VNS lead revision is effective at decreasing the seizure burden to an extent similar to the previous implantation, in agreement with previous reports. More specifically, using the previously utilized segment of vagus nerve for lead revision is as effective as the previous implantation. Among the larger series in the literature, the study in a pediatric population by Agarwal et al. documented treatment efficacy, that is, decreased seizure frequency and severity, similar to that in our series. These authors retrospectively examined the records of 23 patients who underwent VNS lead revision through a combination of techniques and found that the efficacy of the new implant did not appear to be altered by revision surgery. It is unclear in how many cases these authors placed the new electrode on the previously used segment of vagus nerve or on a naive segment. Other smaller studies have also demonstrated a return to previous seizure control with lead revision.

Study Limitations

We demonstrate in a large series of patients the effectiveness of VNS lead revision at the previous site of implantation. However, there are study limitations. As with all retrospective studies, there is inherent bias in our study. A prospective study would better estimate the etiology of lead failure and time to lead failure. Additionally, the widespread use of VNS is recent. The average time to failure and the type of failure may change over time. When analyzing therapeutic success, a regression to the mean should be considered. Seizure frequency fluctuates for many reasons in patients with epilepsy, and this may account for some seizure reduction following lead revision. However, in many of our cases, not only was seizure frequency increased, but interrogation of the VNS system also revealed abnormal impedance, indicating lead failure as well. Other confounding variables include the changing antiepilepsy drugs patients potentially received over the follow-up period. Furthermore, as others have mentioned, the clinical absence of dysphonia or aspiration does not preclude the possibility of vagus nerve injury, and therefore underreporting of actual injury may be present. Further prospective studies of VNS lead revisions will help to elucidate many of these limitations.
Conclusions

Vagus nerve stimulation lead revision surgery with placement of a new electrode at the previously used segment of vagus nerve is effective in decreasing the seizure burden to an extent similar to the initial VNS implant. Even with multiple lead revisions, patients can obtain seizure control similar to that following the initial lead implantation. There is a learning curve with revision surgery, and overall the duration of a revision surgery is longer than the initial implantation. However, complications and infection are rare.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Dlouhy, Viljoen, Kung. Acquisition of data: Dlouhy, Viljoen, Kung, Vogel. Analysis and interpretation of data: Dlouhy, Viljoen, Kung. Drafting the article: Dlouhy, Viljoen. Critically revising the article: Dlouhy, Viljoen, Granner, Howard, Kawasaki. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Dlouhy. Statistical analysis: Dlouhy. Administrative/technical/material support: Granner, Howard, Kawasaki. Study supervision: Dlouhy, Howard, Kawasaki.

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