**Evaluation of the Safety of 10 kHz Spinal Cord Stimulation: Electrical, Histological and Clinical Evidence**

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**Introduction**

High-frequency spinal cord stimulation (SCS) delivering pulses at 10 kHz, as in HF10™ therapy, has been in commercial use in Europe since 2010 and in Australia since 2011. In addition to the evidence supporting the efficacy of this device as reported elsewhere, a multifaceted review of safety of this technology is presented.

**Methods**

The safety of 10 kHz stimulation as delivered by the Senza® system (Nevro Corp., Menlo Park, CA) was assessed with regards to device design and electrical safety, pre-clinical histological studies, long-term and randomized clinical trial results, and physician experience.

**Results**

**Design and Electrical Safety**

Tissue damage occurs as a result of stimulation pulse charge density and charge per phase exceeding the safe range.1-3 Charge per phase and charge density are a function of stimulating electrode size, pulse amplitude and pulse width. HF10 therapy typically has a charge per phase of 0.08 μC/phase and a charge density of 0.6 μC/cm², which are well within the established safe range and much lower than traditional low-frequency SCS (Figure 1).

Tissue damage can also occur from irreversible chemical reactions, which can be mitigated by minimizing charge accumulation.1 Charge accumulation is a function of the type of electrode materials used and the amount of residual charge remaining after each stimulation pulse. The Senza system delivers symmetrical and fully charge-balanced waveforms to inert platinum-iridium electrodes. As validation, a 90 day electrode corrosion bench study was performed (Hagen Scientific, Hopkins, MN), wherein the lead electrodes were subjected to worst case stimulation parameters and compared to a control with no stimulation. This study revealed no corrosion, further validating that there is no charge accumulation at the tissue electrode interface.

**Pre-clinical Histological Evidence**

A caprine histological study of 10 kHz SCS showed no stimulation-related damage to all evaluated structures, including dorsal nerve rootlets, connective tissue, and spinal cord (Figure 2). 12 goats were implanted with 8-contact linear percutaneous leads placed midline in the lumbar epidural space. Six test animals received 10 kHz stimulation for 10 ± 1 days, 24 hours per day.6 Six control animals were also implanted, but no stimulation was applied. Cross sections of lumbar spinal cord, dorsal and ventral roots, and dorsal root ganglia (Figure 2) were examined (Tox Path Specialists, Walkersville, MD). There was no evidence of any neurotoxicity related to prolonged 10 kHz stimulation.

**Clinical Evidence**

In a multicenter study of 72 implanted patients, there was no evidence of neurologic deficit or dysfunction attributable to delivery of HF10 therapy for up to 24 month.5,6 Adverse events were similar in nature and frequency to those seen with traditional low-frequency SCS systems. In the SENZA-RCT pivotal study of 198 implanted patients, a direct 12-month comparison of HF10 therapy to traditional SCS also showed a comparable safety profile (Table 1).

**Physician Experience**

More than 3,000 patients have now received HF10 therapy, some for over 4 years, with no evidence of safety issues regarding 10 kHz stimulation. With over 30,000 cumulative device implant months, there have been no device failures associated with the delivery of HF10 therapy, including no lead or battery failures reported. Furthermore, there have been no reports of stimulation-related neurological deficits associated with HF10 therapy.

**Table 1. Key safety results from the SENZA-RCT study.**

- *Test subject death due to hepatocellular carcinoma at month 13; Control subject death due to myocardial infarction during IPG implant procedure.*

<table>
<thead>
<tr>
<th>Test</th>
<th>Subjects with AEs (N=198)</th>
<th># of AEs</th>
<th>Study-Related SAEs</th>
<th>Unanticipated Adverse Device Effects</th>
<th>Deaths*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF10</td>
<td>198</td>
<td>20 (1.0%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TLC</td>
<td>198</td>
<td>20 (1.0%)</td>
<td>0</td>
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</tbody>
</table>

**Conclusions**

SCS devices delivering HF10 therapy were designed specifically to safely deliver 10 kHz stimulation. Pre-clinical histological studies, long-term and randomized clinical trial results, and physician experience support the safety of this therapy.

**References**


The Senza System in an investigational device in the U.S. Preclinical and clinical studies supported by Nevro Corp.