The "TENS" device used by this Investigator is actually a HakoMed PROElectDT 2000. Written Proof available.

2017 Summary
Clinical Trial Results
NCT # 01979367

Lower Extremity Neurological Ischemia
NCT #01979367

January 19th, 2018

Clinical Trial Policy Site:
[redacted]

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Board Certified, Anesthesiology
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Dear AASEM Board:

The FDA defines a Pivotal Study as

> "…a definitive study in which evidence is gathered to support the safety and effectiveness evaluation of the medical device for its intended use."
>
> *Food and Drug Administration Guidance Document: Design Considerations for Pivotal Clinical Investigations for Medical Devices*

ABSTRACT

INTRODUCTION:
The AASEM sponsored Physician's Clinical Trial Policy NCT # 01979367 is powered according to the Primary Objective of demonstrating non-inferiority of the devices in question (Axon II 250 Hz small pain fiber (spf) testing device, Anodyne/MIRE, TENS, NBPM {Nerve Block pain management}). If non-inferiority is demonstrated via positive responses to the Trial interventions, superiority of the testing devices and therapeutic interventions can be assessed secondarily.

OBJECTIVE:
Enrolling eligible patients aged 50-90 that suffer from painful and debilitating conditions of the lower extremities, such as decreased peripheral blood flow, dependent rubor, swelling, edema, burning, numbness, tingling, loss of sensation, restless legs, and poor balance/ altered gait disturbance. We hypothesize the vast majority of these symptoms correlate strongly with the deterioration/dysfunction of the A-Delta small pain fiber (spf)/nerves in the lower extremities. If our assumption is correct, then identification of the extent of dysfunctional A-Delta nerves and subsequent restoration of normal function of these nerves will lead to overall symptomatic improvement, return of sensory perception and proprioception, pain reduction, and gait stabilization.

METHODS:
Utilizing the Axon II to measure the amplitude response of the lower extremity branches of spinal cord nerve roots (L1,L2,L3,L4,L5,S1,S2 bilaterally) to stimulation at the specific firing frequency of the small pain fibers (250 Hertz), we were able to document the qualitative dysfunction of the A-Delta spf (normal response range is 12-30, with responses >40 deemed strongly indicative of dysfunction, 95% confidence) as the Objective measure of Admittance to the Study.

We aimed to prove the efficacy of the Study Interventions directed at restoring A-Delta spf to normal ranges of qualitative function. The Protocol consisted of 8 sessions of 50 minutes of combined therapy (TENS/MIRE) applied both at the nerve root and the lower extremity of the identified dysfunctional nerves. Therapy was administered at maximal tolerable intensities M-W-F for 3 weeks, with follow-up nerve studies to document Objective response. To sustain the patient through the rather painful nerve reawakening process, and to allow for progressive ramping up of

intensity of therapy at each subsequent visit, we provided NBPM via 8-10 cc's of lidocaine/bupivacaine (w/o epi) after each session.

Other measures such as reductions in VAS pain score, return of sensation (pinprick, vibration perception threshold), reductions in peripheral edema (0, 1+, 2+ scale), improved peripheral circulation (dorsalis pedis pulse strength, capillary refill time, skin temperature), reductions in Restless Leg Syndrome(frequency and intensity, patient report), Restoration of Balance (heel-toe walking capability), and daily increased Ambulatory Capacity (patient report) are all encompassed in our Subjective Endpoints.

RESULTS:

Out of 189 patients enrolled at our site, 159 qualified for the Study. Of these 159 patients, a total of 322 nerves were studied. Out of the 256 fully completed Axon II spf tests, 215 of these 256 nerves studied showed a collective overall improvement of >84%. Patients who responded positively also manifested dramatic Subjective responses as well, with all patients reporting at least 60% reduction in VAS pain scores, and over 90% reporting subsequent normalization of gait, return of sensory perception and proprioception, and near elimination of Restless Legs.

DISCUSSION:

According to the CDC, over 800,000 patients are hospitalized each year due to slips and falls, with over 300,000 hip fractures occurring each year as a result. The costs to Medicare for all these hip fractures, traumatic head injuries, hospitalizations, and convalescent care were over $31 Billion in 2016 alone. Since collectively those patients have a >27% chance of dying within one year, and >50% experience a significant functional decline in the same time frame (CDC data), obviously this means prevention of the fall itself is the key to quality and quantity of life, as well as monumental monetary savings for Medicare.

With the current "narcotic crisis" gripping America, non-narcotic treatment regimens for neuropathic pain conditions that are **safe and efficacious** should be embraced wholeheartedly, by patients, physicians, and payors alike. Even the much utilized, non-narcotic, neuropathic pain medications such as the Gabapentanoids, SNRI's, and TCA's, have well-established serious side effects in the elderly population. Furthermore, regular usage of even Acetaminophen and NSAID's carry substantial liver, kidney and GI risks, respectively, in the elderly. **Therefore, non-narcotic, non-pharmaceutical treatment regimens for these extremely debilitating neurological ischemia/neuropathic pain conditions should be aggressively sought after.**

For patients suffering from disease processes such as Neurological Ischemia, Restless Legs, Neuropathic pain, lack of proprioception, and Altered Gait/Balance Issues (all predisposing factors that lead to those frequent falls), and there being no accepted non-pharmaceutical treatment regimens in the current literature, the combination of Axon II confirmation testing of A-Delta spf nerve dysfunction followed by MIRE/TENS/NBPM therapeutic interventions to correct the underlying sensory deficits certainly appears to be an extremely viable treatment option for these debilitating, life-threatening, and very costly conditions.

This Study Protocol, with an Objective response rate of 84% and a Subjective response rate of at least 60%, and in most cases, almost 90%, establishes that these types of interventions as very attractive indeed. While these results are extremely strong, ongoing data is needed in order to reach a conclusion with a greater confidence interval.

Respectfully Submitted,

[redacted]
Principal Investigator
NCT # 01979367