PROSPECT: PROSPECTIVE STUDY FOR SYMPTOMATIC RELIEF OF ESSENTIAL TREMOR WITH CALA THERAPY

PROTOCOL ET-14
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CLINICAL STUDY SYNOPSIS

Study Objective	
Title	PROSPECT: PROspective study for SymPtomatic relief of Essential tremor with Cala Therapy
Study Device	Cala TWO Device
Objective	The study objective is to evaluate symptomatic hand tremor relief in the treated hand following stimulation with the Cala TWO device in adults with essential tremor over a 3-month duration

Study Design Elements	
Study Design	Prospective, multi-center, single-arm, non-significant risk study designed to evaluate the Cala TWO device. Subjects will be screened for eligibility and fitted with a Cala TWO device. Subjects will wear the device at home for a period of 3 months, during which they will be asked to stimulate their dominant hand twice a day. The stimulation amplitude will be based on each subject's stimulation threshold. Subjects will have in clinic assessments at enrollment, month 1 and 3.
Effectiveness Endpoints	The effectiveness of the Cala TWO device in reducing essential tremor symptoms will be evaluated by the following: <u>Co-Primary Effectiveness Endpoints</u> • TRG Essential Tremor Rating Assessment Scale (TETRAS) subset score, relevant to the stimulated upper limb, change from pre-stimulation at baseline to post-stimulation at 3 months. • Bain & Findley Activities of Daily Living (ADL) scale subset score, relevant to the stimulated upper limb, change from pre-stimulation at baseline to post-stimulation at 3 months. <u>Secondary Effectiveness Endpoint</u> • Tremor power, as collected with the device during postural holds, change from pre-stimulation to post-stimulation across sessions. <u>Additional Exploratory Analyses</u> • Quality of Life in Essential Tremor Questionnaire (QUEST) • Clinician/Patient Global Impression of Severity (C/PGI-S) • Clinician/Patient Global Impression of Improvement (C/PGI-I) • Patient Session Impression of Improvement (PSI-I) • TETRAS – subset relevant to non-stimulated upper limb • TETRAS and ADL pre- versus post-stimulation within each visit • Product Survey • Device usage metrics
Safety Endpoint	The safety of the Cala TWO device will be evaluated by the incidence of device and therapy-related adverse events. Additionally, all adverse events documented during study conduct will be tabulated and reported.

Number of Subjects	Up to 500 subjects
Number of Sites	Up to 40 US sites
Study Participation	The length of study participation is 3 months +/- 2 weeks
Follow-up Schedule	Enrolled subjects will return to the site at 1 month +/- 1 week and 3 months +/- 2 weeks from enrollment

Subject Population	
Inclusion Criteria	Prospective subjects must meet all of the following criteria to be eligible for study participation: • Must be ≥22 years of age • Competent and willing to provide written, informed consent to participate in the study • A diagnosis of essential tremor as confirmed from clinical history and examination by a movement disorder neurologist • A tremor severity score of 2 or above in the dominant hand/arm as measured by any one of the TETRAS upper limb items and a minimum subset score of 6 across all upper limb items • Significant disability due to essential tremor (Bain & Findley score of 3 or above in any one of the upper limb items and a minimum subset score of 8 across all upper limb items) • Stable dose of tremor medications, if applicable, for 30 days prior to study entry • Stable dose of antidepressant medications, if applicable, for 90 days prior to study entry • Willing to comply with study protocol requirements including: o remaining on a stable dosage of tremor and antidepressant medications, if applicable, during the duration of the study o no significant alcohol or caffeine consumption within 8 hours prior to study visits o no usage of the Cala TWO device within 8 hours prior to study visits
Exclusion Criteria	Prospective subjects who meet any of the following criteria are not eligible for enrollment in this study: • Moderate to severe ethanol dependence as defined by the criteria outlined in the DSM-5 (score of 4 or higher)

	• Implanted electrical medical device, such as a pacemaker, defibrillator, or deep brain stimulator, or implanted metal in the wrist to be stimulated • Previous thalamotomy procedure, including stereotactic thalamotomy, gamma knife radiosurgical thalamotomy, and focused ultrasound for the treatment of tremor • Suspected or diagnosed epilepsy or other seizure disorder • Swollen, infected, inflamed areas, or skin eruptions, open wounds, or cancerous lesions of skin at stimulation site • Peripheral neuropathy affecting the tested upper extremity • Presence of any other neurodegenerative disease like Parkinson-plus syndromes suspected on neurological examination. These include: multisystem atrophy, progressive supranuclear palsy, dementia with Lewy bodies, and Alzheimer's disease. • Anyone suspected to have the diagnosis of idiopathic Parkinson's disease (PD). This includes excluding anyone with the presence of parkinsonian features including bradykinesia rigidity, or postural instability. Subjects who exhibit only mild resting tremor but no other symptoms or signs of PD may be included. • Botulinum toxin injection for hand tremor within 6 months prior to study enrollment • Are participating or have participated in another interventional clinical trial in the last 30 days which may confound the results of this study, unless approved by the Sponsor • Significant alcohol or caffeine consumption within 8 hours prior to study enrollment, which may confound the results of the study, where significant caffeine is considered more than 95 mg (equivalent to a cup of coffee), and significant alcohol is considered more than 14 g (equivalent to 5 oz of wine, 12 oz of beer, or 1.5 oz of distilled spirits). • Subjects unable to communicate with the investigator and staff • Any health condition that in the investigator's opinion should preclude participation in this study • Pregnancy or anticipated pregnancy during the course of the study

Study Contacts	
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