EXCITE: A PILOT STUDY TO EVALUATE THE SAFETY AND INITIAL EFFECTIVENESS OF THE CALA ONE DEVICE TO REPEATABLY AID IN THE SYMPTOMATIC RELIEF OF ESSENTIAL TREMOR

PROTOCOL ET-13
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EXCITE: A Pilot Study to Evaluate the Safety and Initial Effectiveness of the Cala ONE Device to Repeatably Aid in the Symptomatic Relief of Essential Tremor
ET-13

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CLINICAL STUDY SYNOPSIS

Study Objective	
Title	A Pilot Study to Evaluate the Safety and Initial Effectiveness of the Cala ONE Device to Repeatably Aid in the Symptomatic Relief of Essential Tremor
Study Device	Cala ONE Device
Objective	The study objectives are: - To evaluate the safety and initial effectiveness of the Cala ONE device to repeatably aid in the symptomatic relief of hand tremors in adults with essential tremor - To evaluate the feasibility of two different types of controls (sham and 'no intervention') and their corresponding endpoints for future randomized controlled trials in the home environment

Study Design Elements	
Study Design	Prospective, multi-center, randomized, controlled study designed to evaluate safety and repeatable effectiveness. Subjects will be randomized 2:1:1 to transcutaneous afferent patterned stimulation (TAPS), sham (zero-amplitude stimulation), or 'no intervention', respectively. Subjects randomized to the TAPS and sham arms will be blinded to their randomization assignments for the first 2-3 weeks of participation (controlled phase). After the first 2-3 weeks, all subjects will be crossed over to TAPS (open-label phase) for 2-3 weeks. During study participation, all subjects are to remain on a stable dosage of medications prescribed for the treatment of essential tremor, if applicable.
Effectiveness Assessments	The effectiveness of the Cala ONE device in reducing essential tremor symptoms will be evaluated by analyzing the following: In-office physician-rated assessments: - Clinical Rating Scale for Tremor (CRST) - Clinical Global Impression of Severity (CGI-S) - Clinical Global Impression of Improvement (CGI-I) Subject-rated assessments (in-office and at-home): - Bain & Findley Activities of Daily Living (ADL) Scale - Quality of life in Essential Tremor Questionnaire (QUEST) - Patient Global Impression of Severity (PGI-S) - Patient Global Impression of Improvement (PGI-I) - Subject survey of satisfaction and durability of effect (i.e. on average how long tremor relief lasts after a stimulation session)

	Device-related assessments: - Motion data collected by the device during lateral postural holds in the home environment - Device usage metrics (e.g. number of stimulation sessions completed daily or changes in stimulation amplitude) The following measures will be evaluated between the treatment and sham arms during the controlled phase of the study: - In-office physician-rated assessments pre, during and post TAPS, compared to pre, during and post sham stimulation - In-office subject-rated assessments pre, during and post TAPS, compared to pre, during and post sham stimulation - At-home subject-reported assessments pre and post TAPS, compared to pre and post sham stimulation - Device-related assessments pre and post TAPS, compared to pre and post sham stimulation The following measures will be evaluated between the treatment and 'no intervention' arms during the controlled phase of the study: - In-office physician-rated assessments post TAPS compared to 'no intervention' - In-office subject-rated assessments post TAPS compared to 'no intervention' - At-home subject-reported assessments post TAPS compared to 'no intervention' The following measures will be evaluated in the open-label phase of the study: - In-office physician-rated assessments pre, during and post TAPS - In-office subject-rated assessments pre, during and post TAPS - At-home subject-reported assessments pre and post TAPS - Subject satisfaction survey - Device-related assessments
Safety Endpoints	The safety of the Cala ONE device will be evaluated by the incidence of device and therapy-related adverse events
Number of Subjects	Up to 70 subjects
Number of Sites	Up to five sites
Study Participation	The length of study participation is up to 6 weeks.
Blinding	The first 2-3 weeks of the study are double-blinded for the treatment and sham arms. The subjects and rating movement disorder neurologists will be blinded to the therapy allocation for the treatment and sham arms. The subjects in the 'no intervention' arm and their rating neurologists will not be blinded to their therapy allocation. The last 2-3 weeks are open-label, and all subjects will be given the option to use the Cala ONE device.

Subject Population	
Inclusion Criteria	Prospective subjects must meet all of the following criteria to be eligible for study participation: • Must be ≥22 and ≤80 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 • Postural, action or intention tremor severity score of 2 or above in the dominant hand/arm as measured by the CRST rating scale • Significant disability due to essential tremor (Bain & Findley score of 3 or above in any one of the hand items) • Currently or previously prescribed either propranolol or primidone for the treatment of essential tremor • Stable dose of tremor medications for 30 days prior to study entry • Stable dose of antidepressant medications 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 12 hours of study visits o no significant alcohol or caffeine consumption within 4 hours of twice-daily at home assessments during the controlled phase of the study

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 • 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 • Are participating or have participated in another Cala Health clinical trial • Significant alcohol or caffeine consumption within 12 hours of 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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