Electrical Stimulation of the Dentate Nucleus area (EDEN) for Improvement of Upper Extremity Hemiparesis due to Ischemic Stroke: A Safety and Feasibility Study

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Sponsor Information:
Enspire DBS Therapy, Inc.
2 Oliver St. STE 616
Boston, MA 02446

Contact Person:
[redacted]

PROTOCOL SYNOPSIS

Electrical Stimulation of the Dentate Nucleus area (EDEN) for Improvement of Upper Extremity Hemiparesis due to Ischemic Stroke: A Safety and Feasibility Study	
Study Overview	
Study Objective	The objective of this study is to document the safety and patient outcomes of electrical stimulation of the dentate nucleus area for the management of chronic, moderate to severe upper extremity hemiparesis due to ischemic stroke. The proposed study is a first in human safety and feasibility study intended to provide preliminary data to design a future pilot study.
Test Device	Boston Scientific, Inc. Vercise™ Deep Brain Stimulation System.
Investigational Treatment	Unilateral electrical stimulation of the cerebellar dentate nucleus on the side ipsilateral to the hemiparesis (contralesional to stroke).
Study design	
Study Design	Prospective, open-label, single arm, safety and feasibility study
Control	Due to heterogeneity of ischemic stroke, each patient will serve as his or her own control. Comparison will be made across time (e.g. rehabilitation vs. test, and follow-up)
Investigative Sites	One site (Cleveland Clinic).
Number of Subjects	Up to 12 subjects implanted.
Patient Population	Survivors of an initial ischemic stroke between 12 and 36 months post stroke with residual severe unilateral, upper extremity hemiparesis defined as ≤ 42 on the upper extremity subscale of the Fugl-Meyer Assessment.
Primary Endpoint	The primary endpoint will be the incidence of all serious adverse events, including Serious Adverse Events (SAEs), Serious Adverse Device Events (SADEs), and Unanticipated (Serious) Adverse Device Events (UADE), from the time of enrollment through follow-up. All serious adverse events will be further categorized as procedure-, DBS device-, and stimulation-related.

	All non-serious adverse events will also be tabulated and reported.
Secondary Endpoints	• Arm Motor Ability Test (AMAT) • Bilateral Box and Block Test (BBT) • Bimanual Grip strength test • EuroQol (EQ-5D) • Fugl-Meyer Assessment, Upper Extremity (FMA-UE) • 9-Hole Peg Test • Short Form Health Survey (SF-12) • Modified Ashworth
Other Endpoints	• Beck Anxiety Inventory (BAI) • Beck Depression Inventory (BDI) • PET • Local Field Potentials • TMS Motor Maps • H-reflex • TMS Cerebellar Brain Inhibition (CBI)
Statistical Hypothesis	No formal statistical hypotheses are proposed for this feasibility study.
Study Phases	
Study Phases Summary	• Baseline • DBS Implant Procedure • Postoperative Recovery (4 weeks) • Rehab Baseline (8 weeks) • DBS Programming (4 to 10 weeks) with rehab continuation • Testing: Stimulation of the dentate nucleus + Rehab (16 weeks) • Rehab Follow-up (4 weeks) • Long Term Follow-up • DBS Explant Procedure • Explant Follow-up (4 weeks)
Rehabilitation Program	All patients will undergo an outpatient rehabilitation program after postoperative recovery. The frequency and duration of therapy sessions will be two times per week for 1-1.5 hours of treatment time over a 2-hour scheduled contact interval. In addition to the formal outpatient therapy sessions, participants will sign a behavioral contract that obligates them and their caregivers to continue with their upper extremity rehabilitation program, as specified by the treating therapist, at home.

Testing (Test Treatment + Rehab)	Subjects will receive stimulation of the dentate nucleus area and continue their ongoing rehabilitation program (test treatment + rehab) for 16 weeks.
Rehab Follow-up	Once the testing phase (test treatment + rehab) has concluded, investigators will gradually wean OFF the device. This will be to assess if gains achieved during the testing phase will persist without continuous stimulation. Loss of more than 50% of improvements achieved during the testing phase will prompt the investigators to turn the devices back ON. Improvements will be indexed with sub-scores (proximal, distal and total limb) of the Fugl-Meyer Scale. Subjects will continue their ongoing rehabilitation program for 4 weeks.
Long-term Follow-up and Study Completion	Once the Rehab Follow-up phase is completed, subjects will be followed until their one-year post implant follow-up. There will be no mandatory structured rehabilitation provided by the study and the device will remain OFF until explanted during this phase. Then the device will be explanted as per study procedure. Subjects will have a final follow up visit 6-month post explant. At the conclusion of the 6-month post explant follow-up the subject will have completed this protocol.