Medical Device Clinical Trial Protocol

Protocol No.: FSK-CIP-2

Assessment of a novel NeuroAI-powered transcutaneous neuromodulation device in alleviating tremor symptoms and enhancing quality of life for patients with upper limb essential tremor (TRANQUIL)

Name of the investigational product: Felix™ NeuroAI™ Wristband

Model and specification: Please see the IFU for details.

Protocol version No. and date: [redacted], July 12, 2024

Sponsor: Hangzhou Fasikl Technology Co., LTD

Fasikl Incorporated

CONFIDENTIALITY STATEMENT

All information contained in this protocol is the property of Hangzhou Fasikl Technology Co., LTD and Fasikl Incorporated. Therefore, this protocol is only provided to investigators, co-investigators, ethics committees, regulatory authorities and other relevant medical institutions for review. Without the written approval of Hangzhou Fasikl Technology Co., LTD and Fasikl Incorporated, it is strictly forbidden to communicate any information contained in this protocol to any third parties not related to this study, except for the necessary explanation to the potential participants when signing the informed consent form (ICF) with them.

COMPLIANCE STATEMENT

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki and the applicable regulatory requirements (such as, 21 CFR Part 50, 21 CFR Part 56,21 CFR Part 812, 21 CFR Part 54, and 21 CFR Part 11, GCP). The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB) of the respective investigational site.

INVESTIGATOR'S STATEMENT

I agree:

1. I will implement, conduct and finalize this clinical investigation in compliance with the Clinical Investigation Plan, Good Clinical Practices, and all other applicable regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB) or conditions of approval by the reviewing Independent Ethics Committee (IEC), Declaration of Helsinki, and all country specific laws and regulations where applicable.

2. To accurately record all data required into the electronic case report form (eCRF) and complete the final report of the clinical study on time.

3. The investigational medical device is only used in this clinical study. The receipt and use of the study device will be completely and accurately recorded, and the records will be kept during the clinical study.

4. To allow the clinical research associate (CRA), monitor and supervision department authorized or designated by the Sponsor, auditor or regulatory authority to monitor, audit and inspect the clinical study.

5. To strictly perform the clinical study contract and articles of agreement signed by all parties.

I have read the CIP, including the above Statement and fully agree to all requirements.

Comments of the Principal Investigator	
Signature (Seal)	[redacted]
Date	

Comments of the Medical Device Clinical Study Institution	
Signature (Seal)	[redacted]
Date	

Comments of the Sponsor	
Signature (Seal)	[redacted]
Date	

Contents

List of abbreviations

Abbreviation	English name
AE	Adverse Event
ADE	Adverse Device Effects
ADL	Activities of Daily Living
AUD	Alcohol Use Disorder
BMI	Body Mass Index
CFR	Code of Federal Regulations
CGI-I	Clinical Global Impression of Improvement
CGI-S	Clinical Global Impression of Severity
CIP	Clinical Investigation Plan
CRF	Case Report Form
DBS	Deep Brain Stimulation
DSM-5	Diagnostic and Statistical Manual of Mental Disorders Fifth Edition
EDC	Electronic Data Capture
ET	Essential Tremor
FDA	Food and Drug Administration
HIFU	High-Intensity Focused Ultrasound
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IFU	Instructions for Use
IMU	Inertial Measurement Unit
ITT	Intend to Treat
IRB	Institutional Review Board
mITT	Modified Intent to Treat
MRgFUS	Magnetic Resonance-guided Focused Ultrasound
PGI-I	Patient Global Impression of Improvement
PGI-S	Patient Global Impression of Severity
PPS	Per-Protocol Set
QoL	Quality of Life
QUEST	Quality of Life in Essential Tremor Questionnaire
SADE	Serious Adverse Device Effects
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

Abbreviation	English name
TAPS	Transcutaneous Afferent Patterned Stimulation
TETRAS	Tremor research group Essential Tremor Rating Assessment Scale
UADE	Unanticipated adverse device effect
USADE	Unanticipated Serious Adverse Device Effect
VIM	Ventral intermediate nucleus of the thalamus

Synopsis

Protocol title	Assessment of a novel NeuroAI-powered transcutaneous neuromodulation device in alleviating tremor symptoms and enhancing quality of life for patients with upper limb essential tremor
Short title	TRANQUIL
Protocol number	FSK-CIP-2
Study Objective	The objective of this clinical investigation is to evaluate the effectiveness and safety of the Felix™ NeuroAI™ Wristband to aid in the relief of upper limb tremor in adults with essential tremor (ET).
Investigational Devices	Felix™ NeuroAI™ Wristband
Trial design	This study is a prospective, randomized, sham-controlled, double-blinded, multi-center, multi-region trial. There will be two phases in the study: • Randomized Phase (baseline to 90 days): Approximately N=120 subjects will be randomized in a 2:1 ratio to either the Felix group or Sham Stimulation group. Data from the randomized phase will be used to support regulatory application. • Continued Access Phase (90 days to 1 year): All patients in the randomized phase will be encouraged to participate in the continued access phase. Subjects randomized to the Sham arm will be crossed over to Felix stimulation. Data from the continued access phase will be used to support insurance coverage and medical guideline.
Primary efficacy endpoints	Primary Endpoint: Change in Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) modified Activities of Daily Living (mADL) score from baseline pre-stimulation to Day 90, Superiority of Felix vs. Sham stimulation. TETRAS mADL score is a composite sum of items 2 to 11 of the TETRAS ADL subscale and items 6 (bilateral) and 7 (dominant hand) of the TETRAS Performance subscale. TETRAS mADL score is calculated as the sum of all 12 items and ranges from 0 to 52.
Secondary Endpoints	**1) Secondary mADL endpoints** • Change in TETRAS mADL score from baseline pre-stimulation to 14 days, 30 days, and 60 days. Felix vs. sham stimulation. • For the Felix arm, change in TETRAS mADL score from baseline pre-stimulation to 180 days and 1 year. • For the sham arm, change in TETRAS mADL score from 90 days to 180 days and 1 year. • The proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified margin (in the statistical analysis plan, SAP), from baseline pre-stimulation to 14 days, 30 days, 60 days, and 90 days. Felix vs. sham stimulation. • For the Felix arm, the proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified

	margin (in the SAP), from baseline pre-stimulation to 180 days and 1 year. • For the sham arm, the proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified margin (in the SAP), from 90 days to 180 days and 1 year. **2) Physician-rated assessments (in-clinic):** • TETRAS Performance Subscale (items 1, 4 and 8) Collect and record the scores of TETRAS Performance Subscale (items 1, 4 and 8) at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year. • TETRAS Performance Subscale (items 6 and 7) Collect and record the scores of TETRAS Performance Subscale (items 6 and 7) at baseline pre-stimulation, baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. • TETRAS Dominant Hand Score Defined as the total scores of TETRAS Performance Subscale for the dominant hand (items 4, 6, 7 and 8) at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year. • Clinical Global Impression of Severity (CGI-S) Collect and record the scores of CGI-S at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year. • Clinical Global Impression of Improvement (CGI-I) Collect and record the scores of CGI-I at baseline post-stimulation, 30 days, 90 days and 1 year. **3) Subject-rated assessments (in-clinic and at-home):** • TETRAS ADL Subscale Collect and record the scores of TETRAS ADL Subscale at baseline pre-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. • Patient Global Impression of Severity (PGI-S) Collect and record the scores of PGI-S at baseline pre-stimulation, baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. • Patient Global Impression of Improvement (PGI-I) Collect and record the scores of PGI-I at baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. • Quality of Life in Essential Tremor Questionnaire (QUEST) Collect and record the QUEST at baseline pre-stimulation, 90 days, and 1 year. • Survey of satisfaction and durability of effect (i.e., how long tremor relieve lasts after stimulation) at 14 days, 30 days, 60 days, 90 days, 180 days, and 1 year Collect and record the survey of satisfaction and durability of effect at 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. 4) Investigational device-measured inertial data (continuously measured when the device is powered on) Tremor conditions will be characterized by device-measured inertial data, such as tremor power, tremor amplitude, and tremor frequency and will be analyzed according to the SAP.

Safety Endpoints	1) Adverse events and serious adverse events The types, incidences (%) and frequencies of AEs/SAEs occurring in the clinical trial will be evaluated. 2) Adverse device effects and serious adverse device effects The types, incidences (%) and frequencies of medical device-related AEs/SAEs occurring in the clinical trial will be evaluated. 3) Unanticipated adverse device effect (UADE) and unanticipated serious adverse device effect (USADE) The types, incidences (%) and frequencies of UADEs/USADEs occurring in the clinical trial will be evaluated. 4) Device deficiencies The types, incidences (%) and frequencies of device deficiencies occurring during the clinical trial will be evaluated.
Sample size	Power and sample size analysis: Assumptions: • 2:1 randomization between Felix and sham [redacted] • One-sided alpha of 0.025 Using t-test for two independent samples with equal variances, a total sample size of 120 will provide 92% power.
Number of Subjects Required for Inclusion in Clinical Investigation	Approximately 120 subjects (50% US and 50% China).
Research sites and Principal investigators	Approximately 8 sites in the US and 4 sites in China will participate in the study. See the list of research sites.
Study duration	The primary endpoint requires a 90-days follow up. Long term follow-up will continue up to 1 year.
Subject Follow-up	In-Clinic: Baseline, 30 days, 90 days, 1 year In-Clinic or Virtual: 14 days, 60 days, 180 days This study consists of 7 visits, including: Visit 1 (screening, -7 days-Day 1; baseline, pre-stimulation/post-stimulation, Day 1, in-clinic), Visit 2 (14 days±3 days, in-clinic/virtual), Visit 3 (30 days±7 days, in-clinic), Visit 4 (60 days±7 days, in-clinic/virtual), Visit 5 (90 days±14 days, in-clinic), Visit 6 (180 days±30 days, in-clinic/virtual), Visit 7 (1 year±30 days, in-clinic).

	A virtual technical support session will be conducted within 1-2 days after Day 1. There will be no clinical assessment. The goal of this session is to ensure patients can properly use the device. Additional virtual technical support session can be scheduled as needed.
Inclusion Criteria	1. At least 18 years of age. 2. Willing to provide written, informed consent to participate in the study. 3. A clinical diagnosis of ET by a movement disorder specialist. 4. For the dominant hand, a tremor severity score of 2 or higher as measured by one of the six TETRAS Performance Subscale (PS) tasks listed below and a total score of 7 or higher across all tasks listed below. If applicable, this must be met while the patient is on ET treatment. a) TETRAS PS Item 4: Upper limb tremor i. Forward outstretched posture ii. Lateral "wing beating" posture iii. Finger-nose-finger b) TETRAS PS Item 6: Archimedes spiral drawing c) TETRAS PS Item 7: Handwriting d) TETRAS PS Item 8: Dot approximation 5. Stable dosage of anti-tremor medications, if applicable, for 30 days prior to study entry. 6. Stable dosage of antidepressant medications, if applicable, for 90 days prior to study entry. 7. Familiar with operating a touch-screen smartphone and connecting to Wi-Fi internet at home. 8. If necessary, have a dedicated caregiver to help with study required activities, such as putting on the study device, etc. 9. Willing to comply with study protocol requirements including: a. Remaining on a stable dosage of anti-tremor and antidepressant medications, if applicable, during the course of the study. b. Do not start any new anti-tremor treatment during the course of the study (except the assigned treatment in the study). c. Remaining on stable caffeine consumption, if applicable, during the course of the study. d. No alcohol or marijuana consumption the day before a study visit. e. Do not share study/device-related information on the internet or with other study patients.
Exclusion Criteria	1. Prior limb amputation or any known symptomatic peripheral neuropathy condition of the involved upper extremity. 2. Prior surgical intervention for ET such as deep brain stimulation or thalamotomy. 3. Moderate to severe alcohol use disorder (AUD) as per Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) (the presence of at least 4 symptoms or more). 4. Any current drug abuse. 5. Use of recreational drugs other than marijuana.

	6. Current unstable epileptic conditions with a seizure within 6 months of study entry. 7. Other possible causes of tremor such as drug-induced tremor, enhanced physiological tremor, dystonia, and Parkinson's disease. 8. Pregnant or nursing subjects and those who plan pregnancy during the course of the study. 9. Swollen, infected, inflamed areas, or skin eruptions, open wounds, or cancerous lesions of skin at the stimulation site. 10. Known allergy to adhesive bandages. 11. The presence of any cognitive or other impairment that in the judgement of the investigator will impede the assessment of study outcomes. 12. Botulinum Toxin injection for hand tremor within 4 months prior to study enrollment. 13. History of use of other transcutaneous afferent patterned stimulation (TAPS) devices such as Cala Trio. 14. Subject is currently participating or has participated in another interventional clinical trial in the last 30 days which may confound the results of this study, unless approved by the Sponsor. 15. Subject is unable to communicate with the investigator and study staff. 16. Any health condition that in the investigator's opinion should preclude participation in this study.

1. SPONSOR INFORMATION

1.1 Name of Sponsor

Hangzhou Fasikl Technology Co., LTD.

Fasikl Incorporated

1.1 Address of Sponsor

[redacted]

1.2 Contact Information of Sponsor

[redacted]

2. PRINCIPAL INVESTIGATOR AND INVESTIGATION SITE(S) INFORMATION

See the principal investigator and investigation site(s) information in the list of the principal investigators and investigation sites separately from the CIP.

3. INTRODUCTION

This clinical investigation will be conducted in accordance with this CIP. All investigators involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

3.1 Background and Rationale

3.1.1 Background

Essential tremor (ET) is a common neurological disorder that often impairs quality of life and may lead to disability and social handicap. It was estimated that approximate 0.9% of people worldwide were affected by ET[18]. The number of patients with essential tremor is more than 10 million in China, and approximately 7 million in the United States[1]. Postural and kinetic tremor seen in ET affects predominately the upper limbs but may also occur in the head, lower limbs, voice, tongue, face, and trunk[2]. Tremor may negatively impact several domains of quality of life including physical such as eating and drinking and psychosocial such as personal relationships and depression[3].

The mechanism producing tremor is unknown in ET but it is thought to arise from the oscillatory activity within a central tremor network, which involves the ventral intermediate nucleus of the thalamus (VIM)[4,5]. Growing evidence suggests that degeneration of Purkinje cells in the cerebellum is involved in the pathophysiology of the condition[6]. Propranolol and primidone are the medications used most frequently and successfully to treat ET, and propranolol is the only medication approved by the US Food and Drug Administration (FDA) for this indication. Unfortunately, 30-50% of patients will not respond to either propranolol or primidone[7]. Moreover, even in first-line drug responders, the reduction in tremor amplitude is only on the order of 50-60%[8]. Second-line medications for ET include topiramate, benzodiazepines, gabapentin, zonisamide, and pregabalin with variable patient responses[2]. For patients who do not respond to medications, current alternative options are invasive neurosurgical procedures, including VIM deep brain stimulation (DBS) and magnetic resonance-guided focused ultrasound (MRgFUS) VIM thalamotomy. These options, while effective for many, carry significant safety risks and expenses associated with invasive procedures[9]. Additionally, there are stringent selection criteria for these surgical approaches such that many patients will not qualify for either procedure.

[redacted]

3.1.2 Rationale for Conducting this Clinical Investigation

[redacted]

Fasikl has conducted a pilot study of the Felix device in both the US (NCT05842434) and China under the same protocol. Between June and September 2023, 12 ET patients were enrolled (7 in the US and 5 in China). All subjects were followed for 7 days (with continuous at home treatment), and average mADL score at the 7-day visit was significantly lower than that at the baseline pre-stimulation (average reduction 8.6 ± 6.2).

This clinical study will evaluate the effectiveness and safety of the Felix™ NeuroAI™ Wristband to aid in the relief of upper limb tremor in adults with essential tremor (ET).

3.2 Investigational Device

3.2.1 Name of the Device(s) Under Investigation

Device name	Model/Type	Serial/Lot Controlled	Manufacturer	Region/ Country	Investigational or Market Released
Felix™ NeuroAI™ Wristband	[redacted]	Yes	Hangzhou Fasikl Technology Co., LTD.	China	Investigational
			Fasikl Incorporated	US	

3.2.2 Description of the Device(s) Under Investigation

The Felix™ NeuroAI™ Wristband (Felix system) is a wrist-worn, noninvasive, transcutaneous neurostimulation system. It is intended to be used by adult patients with ET daily to suppress hand tremors. The device also continuously monitors tremor. The Felix system is composed of the Stimulator, a Connector Band, Electrode Band, Strap, a wireless charger and a mobile app (with the function of artificial intelligence to automatically adjust the stimulation intensity). Figure 1 below provides schematics of the Felix system.

The NeuroAI stimulator contains all the stimulator circuitry, sensors, Bluetooth communication, and battery. The Felix watch has three side pushbuttons for simple controls such as on/off or adjusting stimulation amplitude. Other controls are carried out through the mobile device app.

The user will be fitted with a connector band and an electrode band from several available sizes, depending on their wrist's surface anatomy. The user will be trained to locate their peripheral nerves on the wrist in order to apply the electrode band at the appropriate location. The electrode band sticks to the wrist and provides a direct interface with the user's peripheral nerves. The electrode band is for single use and should be replaced daily.

The connector band magnetically snaps into the watch's back. It provides electrical connections between the stimulator and the electrode band. The user secures the watch around their wrist with the strap.

The charger can be used with any standard USB 2.0 port with at least a 5V/1A power rating. An AC adapter is provided separately. The watch can be charged by placing it sideways (the side without buttons) onto the wireless charger base.

The smartphone app has full control over the stimulator, including starting/stopping stimulation, selecting stimulation parameters, and changing stimulation mode. It connects to the stimulator via Bluetooth. Real-time inertial measurement unit (IMU) data is streamed from the stimulator to the app via Bluetooth. The app can communicate with a secure cloud database to store IMU data and to receive system updates. In AI closed-loop stimulation mode, the app will communicate with a secure cloud AI server to determine the best stimulation setting for the user continuously and control the stimulator accordingly. The user will always be able to pause stimulation manually.

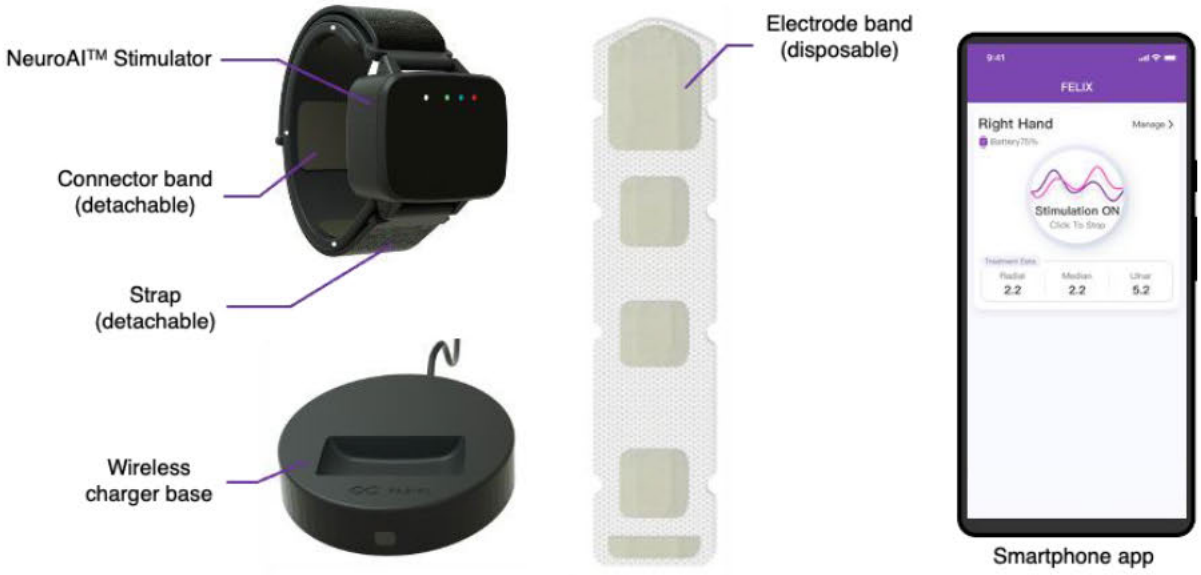


Figure 1. The Felix system

3.2.3 Device Labels and Handling

All current labeling and Instructions for Use (IFU) will be sent under a separate cover to clinical sites.

The Sponsor requires clinical sites to store all investigational products according to the labeling and IFU in a secure area to prevent unauthorized access or use. Dispose of the investigational medical devices according to applicable national regulations and the agreement with the Sponsor after the clinical trial, and special personnel should be responsible for and record the above-mentioned processes. The investigators should not hand over any investigational medical device to any non-participant in the clinical trial.

3.3 Scope of application and relevant information

3.3.1 Indication for Use

[redacted]

3.3.2 Intended population

Adults with essential tremor.

3.3.3 Application site

Wrist.

3.3.4 The way and duration of body contact

Patients can wear the Felix device every day.

3.3.5 Severity and stage of the disease

Upper limb tremors of patient with essential tremor.

3.3.6 Condition for use

Felix™ NeuroAI™ Wristband can be used at a medical institution and at home.

3.3.7 Method of application

Please refer to the product Instructions for Use (IFU) for details.

3.3.8 Contraindication, Warning and Precautions

Please refer to the product IFU for details.

4. STUDY OBJECTIVE

The objective of this clinical investigation is to evaluate the effectiveness and safety of the Felix™ NeuroAI™ Wristband to aid in the relief of upper limb tremor in adults with essential tremor (ET).

5. STUDY DESIGN

This is a prospective, randomized, sham-controlled, double-blinded, multi-center, multi-region clinical trial (MRCT). Approximately 8 sites in the US and 4 sites in China will participate in the study. Each country will enroll approximately 50% of the study population.

This study will consist of two phases:

- Randomized Phase (baseline to 90 days): Approximately N=120 subjects will be randomized in a 2:1 ratio to either the Felix group or Sham Stimulation group. Data from the randomized phase will be used to support regulatory application.
- Continued Access Phase (90 days to 1 year): All the patients in the randomized phase will be encouraged to participate in the continued access phase. Subjects randomized to the Sham arm will be crossed over to Felix stimulation. Data from the continued access phase will be used to support insurance coverage and medical guideline.

Subjects participating in this clinical investigation will be followed for 1 year (±30 days to allow for flexibility in scheduling the last-day visit). The expected duration of enrollment is 7 months. The total duration of the clinical investigation is expected to be 30 months.

6. STUDY ENDPOINTS

6.1 Primary Endpoint

6.1.1 Primary Endpoint

Change in Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)[14, 15] modified Activities of Daily Living (mADL) score from baseline pre-stimulation to Day 90, Superiority of Felix vs. Sham stimulation.

TETRAS mADL score is a composite sum of items 2 to 11 of the TETRAS ADL subscale and items 6 (bilateral) and 7 (dominant hand) of the TETRAS performance subscale (PS). These items are listed below, and the full TETRAS questionnaire is attached in Appendix 1. TETRAS mADL score is calculated as the sum of all 12 items and ranges from 0 to 52.

- TETRAS ADL items (patient rating based on the prior week, each item is rated on a scale from 0 to 4, representing increasing difficulty in doing the activity due to tremor, from normal to severely abnormal/cannot perform the activity):
    - Feeding with a spoon
    - Drinking from a glass
    - Hygiene
    - Dressing
    - Pouring
    - Carrying food trays, plates or similar items
    - Using keys
    - Writing
    - Working (if patient is retired, ask as if they were still working. If the patient is a housewife, ask the question as it relates to housework)
    - Overall disability with the most affected task (name task, e.g. using computer mouse, writing, etc.)
- TETRAS PS items (physician rating, each item is rated on a scale from 0 to 4, representing increasing severity of tremor, from normal to severe):
    - Archimedes spirals (both hands, rated separately)
    - Handwriting (dominant hand)

6.1.2 Rationale for the Primary Endpoint

TETRAS was designed specifically for the clinical measurement of ET severity, requiring no instruments other than a pen and paper. TETRAS ADL scores are rated by the patients based on their assessments of the difficulty in performing common daily activities within one week prior to the assessment. TETRAS PS scores are rated by movement disorder specialists in the clinic as the patients are performing the tasks. The TETRAS ADL and performance scores are highly correlated (correlation coefficient 0.887, $p<0.0001$), and the TETRAS performance items of upper extremity function correlate strongly with transducer measures of upper limb tremor. The scale is brief, valid and highly reliable, making it ideal for ET clinical trials[14].

We have selected the primary endpoint of change in TETRAS mADL score from baseline to 90 days. It provides a comprehensive summary of patients' ability to carry out common daily tasks, as well as physician assessments of spiral drawing and handwriting. Improvement in TETRAS mADL score has a direct impact on ET patients' wellbeing. We have also noticed that TETRAS mADL score was used as the primary endpoint of several contemporary pharmaceutical studies of ET medications (clinicaltrial.gov numbers NCT05021991 and NCT05122650).

6.2 Secondary Endpoints

6.2.1 Secondary mADL endpoints

1) Change in TETRAS mADL score from baseline pre-stimulation to 14 days, 30 days, and 60 days. Felix vs. sham stimulation.
2) For the Felix arm, change in TETRAS mADL score from baseline pre-stimulation to 180 days and 1 year.
3) For the sham arm, change in TETRAS mADL score from 90 days to 180 days and 1 year.
4) The proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified margin (in the statistical analysis plan, SAP), from baseline pre-stimulation to 14 days, 30 days, 60 days, and 90 days. Felix vs. sham stimulation.
5) For the Felix arm, the proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified margin (in the SAP), from baseline pre-stimulation to 180 days and 1 year.
6) For the sham arm, the proportion of patients responding to the treatment, as defined by change in TETRAS mADL score at or above a pre-specified margin (in the SAP), from 90 days to 180 days and 1 year.

6.2.2 Physician-rated assessments (in-clinic):

1) TETRAS Performance Subscale (items 1, 4, and 8)

   Collect and record the scores of TETRAS Performance Subscale (items 1, 4, and 8) at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year. Items 4 and 8 will be rated separately for each limb.

2) TETRAS Performance Subscale (items 6 and 7)

   Collect and record the scores of TETRAS Performance Subscale (items 6 and 7) at baseline pre-stimulation, baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year. Item 6 will be rated separately for each hand. Item 7 will be rated for the dominant hand only.

3) TETRAS Dominant Hand Score

   Defined as the total scores of TETRAS Performance Subscale for the dominant hand (items 4, 6, 7 and 8) at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year.

4) Clinical Global Impression of Severity (CGI-S, Appendix 2)

Collect and record the scores of CGI-S at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days and 1 year.

5) Clinical Global Impression of Improvement (CGI-I, Appendix 2)

Collect and record the scores of CGI-I at baseline post-stimulation, 30 days, 90 days and 1 year.

6.2.3 Subject-rated assessments (in-clinic and at-home):

1) TETRAS ADL Subscale
Collect and record the scores of TETRAS ADL Subscale at baseline pre-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year.

2) Patient Global Impression of Severity (PGI-S, Appendix 3)

Collect and record the scores of PGI-S at baseline pre-stimulation, baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year.

3) Patient Global Impression of Improvement (PGI-I, Appendix 3)

Collect and record the scores of PGI-I at baseline post-stimulation, 14 days, 30 days, 60 days, 90 days, 180 days and 1 year.

4) Quality of Life in Essential Tremor Questionnaire (QUEST, Appendix 4)

Collect and record the QUEST at baseline pre-stimulation, 90 days, and 1 year.

5) Survey of satisfaction and durability of effect (i.e., how long tremor relieve lasts after stimulation, Appendix 5)

Collect and record the survey of satisfaction and durability of effect at 14 days, 30 days, 60 days, 90 days, 180 days and 1 year.

6.2.4 Investigational device-measured inertial data (continuously measured when the device is powered on)

Tremor conditions will be characterized by device-measured inertial data, such as tremor power, tremor amplitude, and tremor frequency and will be analyzed according to the SAP.

6.2.5 Rationale for the Secondary Endpoint

The effectiveness of the investigational medical device will be comprehensively evaluated by TETRAS Performance Subscale, CGI-S, CGI-I, TETRAS ADL Subscale, PGI-S, PGI-I, QUEST, survey of satisfaction and durability of effect and investigational device-measured inertial data. The clinical effectiveness of the investigational medical device can be evaluated through the above indicators.

6.3 Safety Endpoints

6.3.1 Adverse events (AE) and serious adverse events (SAE)

The types, incidences (%) and frequencies of AEs/SAEs occurring in the clinical trial will be evaluated.

6.3.2 Adverse device effects (ADE) and serious adverse device effects (SADE)

The types, incidences (%) and frequencies of medical device-related AEs/SAEs occurring in the clinical trial will be evaluated.

6.3.3 Unanticipated adverse device effect (UADE) and unanticipated serious adverse device effect (USADE)

The types, incidences (%) and frequencies of UADEs/USADEs occurring in the clinical trial will be evaluated.

6.3.4 Device deficiencies

The types, incidences (%) and frequencies of device deficiencies occurring during the clinical trial will be evaluated.

6.3.5 Rationale for the Safety Endpoint

This clinical study will collect the occurrence of AEs, SAEs, ADEs, SADEs, UADEs/USADEs and device deficiencies during clinical trials, and the clinical safety of the investigational medical device can be evaluated through the above indicators.

7. SUBJECT SELECTION AND WITHDRAWAL

7.1 Subject Population

This clinical investigation will enroll adult subjects (at least 18 years of age) of all genders who have experienced tremor in their upper extremity and who have a clinical diagnosis of ET.

7.2 Inclusion and Exclusion Criteria

Assessment for eligibility criteria is based on medical records of the site and interview with a candidate patient. Patients must meet ALL inclusion criteria and NONE of the exclusion criteria to participate in the clinical investigation, otherwise the patient is excluded from the clinical investigation and cannot be enrolled (screen failure).

7.2.1 Inclusion Criteria

1. At least 18 years of age.
2. Willing to provide written, informed consent to participate in the study.
3. A clinical diagnosis of ET by a movement disorder specialist.
4. For the dominant hand, a tremor severity score of 2 or higher as measured by one of the six TETRAS Performance Subscale (PS) tasks listed below and a total score of 7 or higher across all tasks listed below. If applicable, this must be met while the patient is on ET treatment.
    a) TETRAS PS Item 4: Upper limb tremor
        i. Forward outstretched posture
        ii. Lateral “wing beating” posture
        iii. Finger-nose-finger
    b) TETRAS PS Item 6: Archimedes spiral drawing
    c) TETRAS PS Item 7: Handwriting
    d) TETRAS PS Item 8: Dot approximation
5. Stable dosage of anti-tremor medications, if applicable, for 30 days prior to study entry.
6. Stable dosage of antidepressant medications, if applicable, for 90 days prior to study entry.
7. Familiar with operating a touch-screen smartphone and connecting to Wi-Fi internet at home.

8. If necessary, have a dedicated caregiver to help with study required activities, such as putting on the study device, etc.
9. Willing to comply with study protocol requirements including:
    a. Remaining on a stable dosage of anti-tremor and antidepressant medications, if applicable, during the course of the study.
    b. Do not start any new anti-tremor treatment during the course of the study (except the assigned treatment in the study).
    c. Remaining on stable caffeine consumption, if applicable, during the course of the study.
    d. No alcohol or marijuana consumption the day before a study visit.
    e. Do not share study/device-related information on the internet or with other study patients.

7.2.2 Exclusion Criteria

1. Prior limb amputation or any known symptomatic peripheral neuropathy condition of the involved upper extremity.
2. Prior surgical intervention for ET such as deep brain stimulation or thalamotomy.
3. Moderate to severe alcohol use disorder (AUD) as per Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) (the presence of at least 4 symptoms or more).
4. Any current drug abuse.
5. Use of recreational drugs other than marijuana.
6. Current unstable epileptic conditions with a seizure within 6 months of study entry.
7. Other possible causes of tremor such as drug-induced tremor, enhanced physiological tremor, dystonia, and Parkinson's disease.
8. Pregnant or nursing subjects and those who plan pregnancy during the course of the study.
9. Swollen, infected, inflamed areas, or skin eruptions, open wounds, or cancerous lesions of skin at the stimulation site.
10. Known allergy to adhesive bandages.
11. The presence of any cognitive or other impairment that in the judgement of the investigator will impede the assessment of study outcomes.
12. Botulinum Toxin injection for hand tremor within 4 months prior to study enrollment.
13. History of use of other transcutaneous afferent patterned stimulation (TAPS) devices such as Cala Trio.
14. Subject is currently participating or has participated in another interventional clinical trial in the last 30 days which may confound the results of this study, unless approved by the Sponsor.
15. Subject is unable to communicate with the investigator and study staff.
16. Any health condition that in the investigator's opinion should preclude participation in this study.

7.3 Subject Withdrawal and Discontinuation

Each subject meeting all general and screening eligibility criteria shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

(1) Withdrawal as determined by the investigator: When an included subject has any of the following conditions making him/her unsuitable to continue participation in the clinical trial, the investigator will determine that this case should withdraw from the clinical trial:

- Poor compliance with the clinical trial protocol;
- Any SAE or intolerable AE occurring in the clinical trial;
- Some comorbidities, complications or special physiological changes which make the subject unsuitable to continue participation in the clinical trial;
- Any other conditions based on which the investigator determines that the subject should withdraw from the clinical trial.

(2) Voluntary withdrawal from the clinical trial, including the following conditions:

- A subject is unwilling to continue participating in the clinical trial and applies to his/her physician for withdrawal;
- A subject has two missed visits;
- A participant may be discontinued “lost to follow-up” if contact cannot be established over three documented attempts – two phone calls and one written / email.

Sites must notify the Sponsor of the reason(s) for subject discontinuation. Investigators must also report this to their respective IRB as defined by their institution’s procedure(s).

No additional follow-up is required nor will data be recorded from subjects once withdrawn from the clinical investigation.

However, if a subject withdraws from the investigation due to problems related to the safety or performance of the device under investigation, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical investigation.

The research staff will make every effort to contact subjects who are lost to follow-up.

8. INVESTIGATIONAL DEVICE AND CONTROL DEVICE/TREATMENT

8.1 Investigational device

Please find information in Section 3.2 for details.

8.2 Sham device

The sham device will look the same as the Felix device. Instead of generating electrical stimulation through the electrodes, the sham device will generate a brief vibration alert from inside the stimulator case (as illustrated in Figure 2 below). The sham device will deliver the vibration randomly throughout the day, on average one vibration alert every five minutes. Patients in the sham arm will wear the same electrode band and control the device the same way (via the smartphone app) as the Felix arm.

Figure 2. Sham device

9. TREATMENT AND EVALUATION OF ENDPOINTS

The Felix device will continuously collect inertial data from the patient while the device is powered on (regardless of whether stimulation is turned on).

9.1 Study Workflow

Patients who meet all the inclusion and none of the exclusion criteria after screening will be randomized in a 2:1 ratio to either the Felix group or Sham Stimulation group. Figure 3 below shows the process from screening to randomization.

Figure 4 below shows the study workflow. During the baseline visit, patients will first go through pre-stimulation assessments. Next, patients will be fitted with the Felix or sham device(s). For the Felix arm, patients will identify their maximum tolerable stimulation intensity. The sham arm will not go through this process in order to maintain blinding. Patients will be stimulated for 40 minutes. Finally, patients will go through post-stimulation assessments, device training, and be discharged from the clinic.

After discharge from the baseline visit, patients are strongly encouraged to wear the device every day. The device can support full-day AI-controlled closed-loop stimulation. To the extent possible, patients are strongly encouraged to wear the device all day.

Patients will have follow-up visits on 14 days, 30 days, 60 days, 90 days, 180 days, and 1 year. Patients' tremors will be assessed during each visit.

Figure 3. The process from screening to randomization

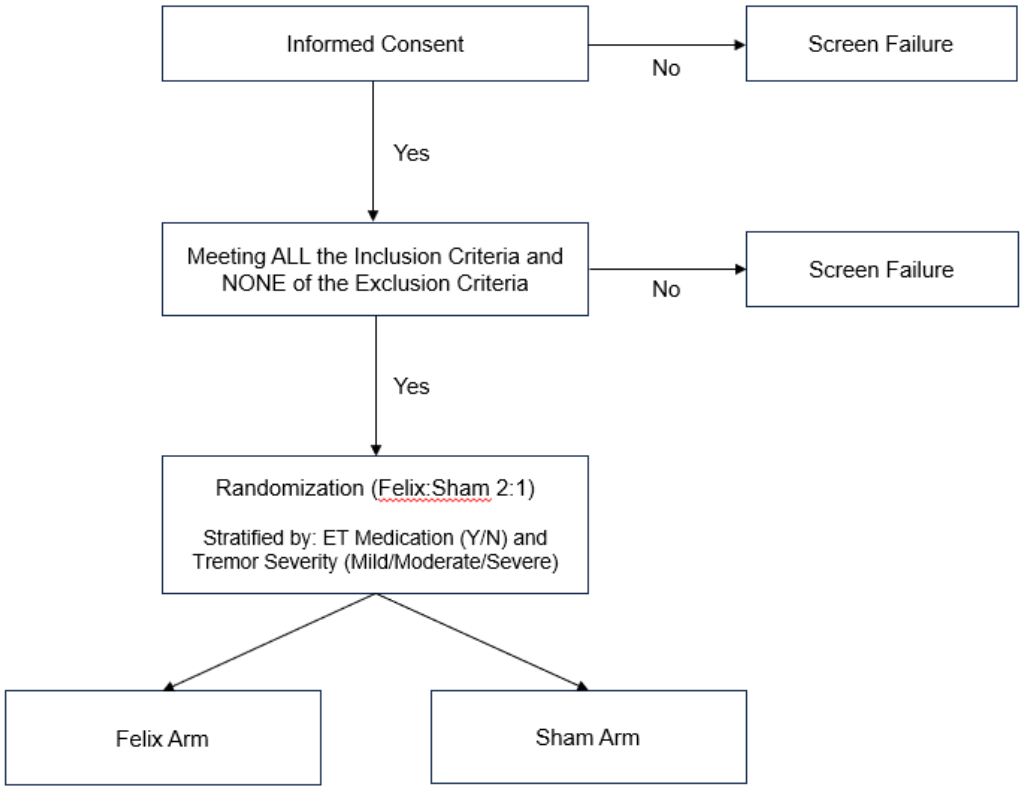
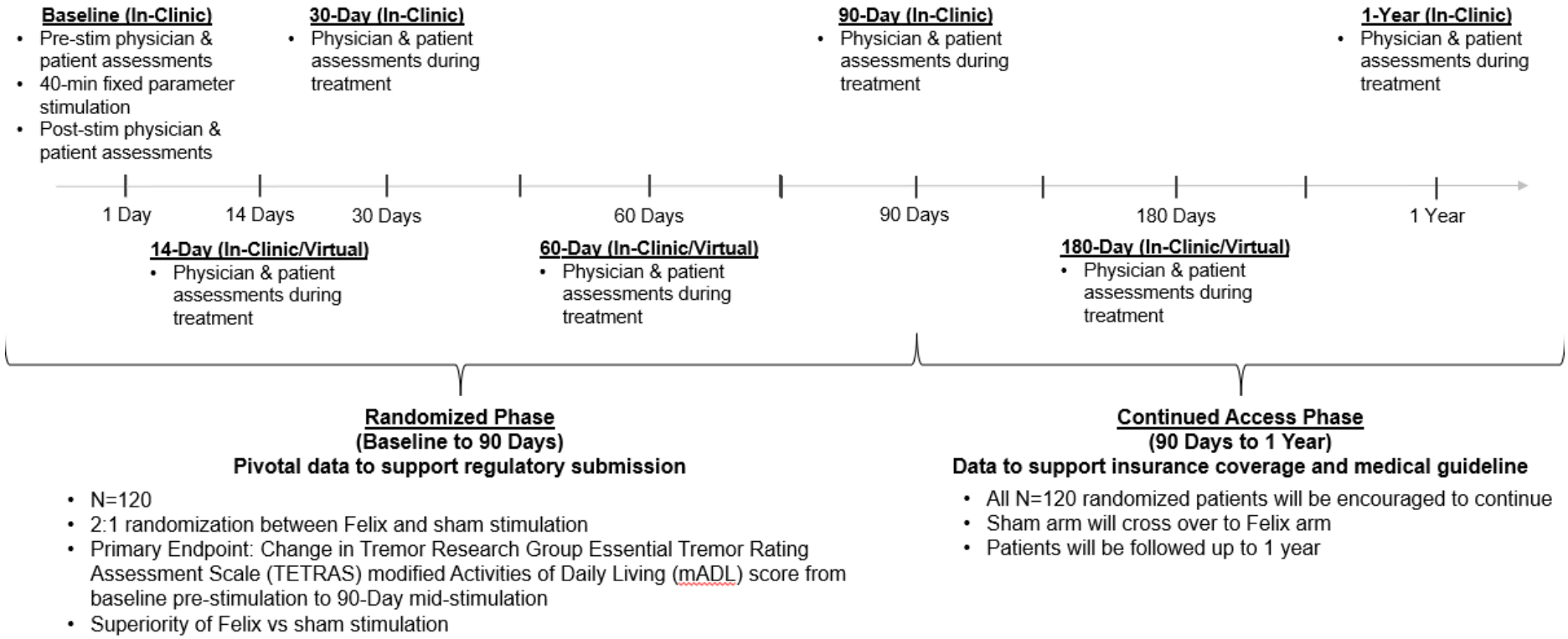


Figure 4. Study Workflow



9.2 Schedule of Events

CIP Activity	Day 1/Baseline Pre-Stimulation (In-Clinic)	Day 1/Baseline Post-Stimulation (In-Clinic)	14 Days (In-Clinic /Virtual)	30 Days (In-Clinic)	60 Days (In-Clinic /Virtual)	90 Days[1] (In-Clinic)	180 Days (In-Clinic /Virtual)	1 Year (In-Clinic)
Visit/Visit window	**V1/-7 days**		**V2/±3 days**	**V3/±7 days**	**V4/±7 days**	**V5/±14 days**	**V6/±30 days**	**V7/±30 days**
Informed Consent	X							
Demographics[2]	X							
Physical Examination[3]	X							
Medical History[4]	X							
Medication[5]	X		X	X	X	X	X	X
Alcohol/marijuana consumption[6]	X		X	X	X	X	X	X
Pregnancy Test[7]	X							
Clinical diagnosis of ET	X							
Check against inclusion and exclusion criteria	X							
Randomization	X							
Device Fitting/Programming[8]	X							
TETRAS Performance Subscale (items 1, 4, and 8)	X	X		X		X		X
TETRAS Performance Subscale (items 6 and 7)	X	X	X	X	X	X	X	X

CGI-S	X	X		X		X		X
CGI-I		X		X		X		X
TETRAS ADL Subscale	X		X	X	X	X	X	X
PGI-S	X	X	X	X	X	X	X	X
PGI-I		X	X	X	X	X	X	X
QUEST	X					X		X
Survey[9]			X	X	X	X	X	X
Adverse Event	X		X	X	X	X	X	X
Protocol Deviation	X		X	X	X	X	X	X
Device Deficiency[10]	X		X	X	X	X	X	X
Withdrawal	X		X	X	X	X	X	X

Notes:

1. Sham arm will cross over to Felix arm at 90 days and go through as steps in 9.3.8, and all subjects will be followed up to 1 year;
2. Demographic data: includes age (date of birth), sex, race, ethnicity;
3. Physical examination: includes height, weight, BMI, body part(s) with tremor;
4. Previous and current medical histories, includes ET onset/diagnosis, family history of ET, ET treatment(s), sensitivity of tremor to alcohol and caffeine, AUD as per DSM-5, history of drug abuse, allergic history, history of tumors, history of other serious diseases (such as symptomatic peripheral neuropathy condition of the involved upper, seizure, Parkinson’s disease and tuberculosis) and surgical history (such as deep brain stimulation or thalamotomy) et al;

5. Record drugs taken include anti-tremor medications and antidepressant medications at pre-stimulation, and current medications; the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded during follow-up;
6. Record alcohol/marijuana consumption at baseline pre-stimulation and alcohol/marijuana consumption the day before a study visit;
7. Urine pregnancy tests at baseline pre-stimulation for all females of childbearing potential;
8. Sites and patients have the option of unilateral stimulation or bilateral stimulation. For unilateral stimulation, the wrist worn will be decided by the investigator and patient together;
9. Survey of satisfaction and durability of effect (i.e., how long tremor relieve lasts after stimulation);
10. User error as well as general issues related to the smartphone itself will not be considered as device deficiency.

For monitoring purposes, all subjects will be prompted to complete a brief patient diary on their smart phone daily during the first week of at-home treatment (Day 1 to 1 year), and weekly after the first week. The diary will include the information in section 9.3.4.

Except for pre-stim physician & patient assessment, other physician & patient assessment will be measured after at least 40-min of stimulation.

9.3 Procedure of the clinical trial

The total duration of this Study includes screening (-7 days-Day 1), baseline pre-stimulation (Day 1), baseline post-stimulation (Day 1) and follow-up period including 14 Days (±3 days), 30 Days (±7 days), 60 Days (±7 days), 90 Days (±14 days), 180 Days (±30 days) and 1 Year (±30 days).

A virtual technical support session will be conducted within 1-2 days after Day 1. There will be no clinical assessment. The goal of this follow-up is to ensure patients can properly use the device. Additional virtual technical support session can be scheduled as needed.

9.3.1 Pre-Stimulation Assessments (V1)

There is a -7 days window to allow for flexibility in scheduling for screening. All subjects will be screened according to the inclusion/exclusion criteria after they or their guardians sign the ICF. This can be conducted at Day 1 or prior to Day 1. Subjects meeting the criteria will be randomized to either the Felix group or Sham Stimulation group. The following visit requirements will be completed at this visit, and information will be analyzed and recorded into CRFs by the sites.

1. Subject demographics: age (date of birth), sex, race, ethnicity;
2. Subject medical history: includes ET onset/diagnosis, family history of ET, ET treatment(s), sensitivity of tremor to alcohol and caffeine, AUD as per DSM-5, history of drug abuse, allergic history, history of tumors, history of other serious diseases (such as symptomatic peripheral neuropathy condition of the involved upper, seizure, Parkinson's disease and tuberculosis) and surgical history (such as deep brain stimulation or thalamotomy) et al;
3. Physical examination: height, weight, BMI, body part(s) with tremor;
4. Record drugs taken include anti-tremor medications and antidepressant medications at pre-stimulation, and current medications;
5. Record alcohol/marijuana consumption;
6. Urine pregnancy tests for all females of childbearing potential;
7. Clinical diagnosis of ET;
8. Physician-rated assessments:
    a) TETRAS Performance Subscale (items 1, 4, 6, 7 and 8, physician rating, each item is rated on a scale from 0 to 4, representing increasing severity of tremor, from normal to severe). The process of this assessment will be videotaped. If patient screening was conducted prior to Day 1, then this set of ratings must be performed again at Day 1.
        - Head tremor
        - Upper limb tremor (both hands, rated separately)
        - Archimedes spirals (both hands, rated separately)
        - Handwriting (dominant hand)
        - Dot approximation task (both hands, rated separately)
    b) Clinical Global Impression of Severity (CGI-S)

9. Subject-rated assessments:
    a) TETRAS ADL items (patient rating based on the prior week, each item is rated on a scale from 0 to 4, representing increasing difficulty in doing the activity due to tremor, from normal to severely abnormal/cannot perform the activity). The process of this assessment will be videotaped:
        - Speaking
        - Feeding with a spoon
        - Drinking from a glass
        - Hygiene
        - Dressing
        - Pouring
        - Carrying food trays, plates or similar items
        - Using keys
        - Writing
        - Working (if patient is retired, ask as if they were still working. If the patient is a housewife, ask the question as it relates to housework)
        - Overall disability with the most affected task (name task, e.g. using computer mouse, writing, etc.)
        - Social Impact
    b) Patient Global Impression of Severity (PGI-S)
    c) Quality of Life in Essential Tremor Questionnaire (QUEST)
10. Device fitting and calibration (by a designated unblinded site personnel, after performing all the assessments above):
    a) Sites and patients have the option of unilateral stimulation or bilateral stimulation. For unilateral stimulation, the wrist worn will be decided by the investigator and patient together.
    b) Subject will be fitted with a connector band and an electrode band based on the location of their peripheral nerves (radial, median, and ulnar nerves) measured according to the instruction provided under a separate cover.
    c) Wash the wrist area where the device will be located according to the IFU provided under a separate cover.
    d) The designated unblinded site staff will obtain the randomized treatment assignment. Sites will follow a standard script in describing the device and potential sensations and why these sensations do not indicate whether the patient is on Felix or the sham device.
    e) Put on the electrode band and the Felix or sham device (with the connector band attached).
    f) For the Felix arm, device fitting will be checked by stimulating individual nerves and confirming the corresponding radiating sensations according to the instructions provided under a separate cover. If needed, select a different sized electrode band and repeat the confirmation step until all three nerves (radial, median, and ulnar nerves) can be properly stimulated.

g) For the Felix arm, identify and record the maximum level of stimulation intensity that causes no discomfort or muscle contraction for each nerve.
h) For the sham arm, steps f) and g) will be skipped in order to maintain patient blinding, i.e., the sham arm patients will be blinded to real stimulation.

9.3.2 Initial Stimulation Session (40 minutes)

Open-loop stimulation will be turned on and the initial stimulation session will last for at least 40 minutes. For the Felix arm, stimulation intensity will be fixed at the maximum comfortable level identified in Step 10 in Section 9.3.1. Unblinded site personnel can help to adjust the intensity if needed.

Stimulation will be turned off after 40 minutes. The device can be powered off and removed.

9.3.3 Post Initial Stimulation Assessments (V1)

Immediately after the initial stimulation session of at least 40 minutes, tremor assessments will be measured. Other following visit contents will be completed during this period, and all information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
   a) TETRAS Performance Subscale (items 1, 4, 6, 7 and 8), as detailed in Section 9.3.1. The process of this assessment will be videotaped.
   b) Clinical Global Impression of Severity (CGI-S)
   c) Clinical Global Impression of Improvement (CGI-I)
2. Subject-rated assessments:
   a) Patient Global Impression of Severity (PGI-S)
   b) Patient Global Impression of Improvement (PGI-I)
3. Adverse Event;
4. Device Deficiency.
5. Patients will be trained on how to apply and use the device and basic troubleshooting. Sites will verify that patients can carry out all the steps (putting on/off the electrode band and the device, device operation, etc.) independently before discharging the patient.

9.3.4 At-Home Treatment

From Day 1 to 1 year, to the extent possible, subjects will wear the Felix device all day every day. The device, while being worn, should always be powered on. Closed-loop stimulation should be turned on at the beginning of the day and can be paused if necessary. To the extent possible, subjects are required to stay in close proximity (within 3 meters or 9 feet) to their smartphone at all times to ensure data transmission. The electrode band will be removed by subjects and discarded every day.

The following steps will be implemented to provide technical support and compliance monitoring:

1. A virtual technical support session will be conducted within 1-2 days after Day 1 clinic visit. There will be no clinical assessment. The goal of this session is to ensure patients

can properly use the device. Additional virtual technical support session can be scheduled as needed.

2. For monitoring purposes, all subjects will be prompted to complete a brief patient diary on their smart phone daily during the first week of at-home treatment, and weekly after the first week. The diary will include the following information:
    a. In the morning before turning on stimulation:
        i. PGI-S
        ii. Pictures of bilateral spiral drawings and handwriting
        iii. Pictures of the front and the back of the wrist area of the treated hand(s) with the device in place on the wrist (for the first week only)
    b. At night after turning off stimulation:
        i. Overall satisfaction with the treatment
        ii. PGI-S and PGI-I
        iii. Pictures of bilateral spiral drawings and handwriting
3. Device operations (such as power on/off, stimulation on/off, Bluetooth connection, internet connection) will be monitored. Patients may receive notifications on their smartphones about device compliance, e.g., the need to stay in close proximity with the smartphone and the need for the smartphone to be connected to the internet (either through Wi-Fi or cellular data).

9.3.5 In-Clinic/Virtual Visit at 14 Days (V2/±3 days)

There is a ±3 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic/virtual visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
    a) TETRAS Performance Subscale (items 6 and 7), as detailed in Section 9.3.1
2. Subject-rated assessments:
    a) TETRAS ADL items, as detailed in Section 9.3.1
    b) Patient Global Impression of Severity (PGI-S)
    c) Patient Global Impression of Improvement (PGI-I)
    d) Survey of satisfaction and durability of effect
3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V2;
5. Adverse Event;

6. Device Deficiency.

9.3.6 In-Clinic Visit at 30 Days (V3/±7 days)

There is a ±7 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
   a) TETRAS Performance Subscale (items 1, 4, 6, 7 and 8), as detailed in Section 9.3.1
   b) Clinical Global Impression of Severity (CGI-S)
   c) Clinical Global Impression of Improvement (CGI-I)
2. Subject-rated assessments:
   a) TETRAS ADL items, as detailed in Section 9.3.1
   b) Patient Global Impression of Severity (PGI-S)
   c) Patient Global Impression of Improvement (PGI-I)
   d) Survey of satisfaction and durability of effect;
3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V3;
5. Adverse Event;
6. Device Deficiency.

9.3.7 In-Clinic/Virtual Visit at 60 Days (V4/±7 days)

There is a ±7 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic/virtual visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
   a) TETRAS Performance Subscale (items 6 and 7), as detailed in Section 9.3.1
2. Subject-rated assessments:
   a) TETRAS ADL items, as detailed in Section 9.3.1
   b) Patient Global Impression of Severity (PGI-S)
   c) Patient Global Impression of Improvement (PGI-I)
   d) Survey of satisfaction and durability of effect;
3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V4;
5. Adverse Event;

6. Device Deficiency.

9.3.8 In-Clinic Visit at 90 Days (V5/±14 days)

There is a ±14 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
    a) TETRAS Performance Subscale (items1, 4, 6, 7 and 8), as detailed in Section 9.3.1. The process of this assessment will be videotaped.
    b) Clinical Global Impression of Severity (CGI-S)
    c) Clinical Global Impression of Improvement (CGI-I)
2. Subject-rated assessments:
    a) TETRAS ADL items, as detailed in Section 9.3.1. The process of this assessment will be videotaped.
    b) Patient Global Impression of Severity (PGI-S)
    c) Patient Global Impression of Improvement (PGI-I)
    d) Quality of Life in Essential Tremor Questionnaire (QUEST)
    e) Survey of satisfaction and durability of effect;
3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V5;
5. Adverse Event;
6. Device Deficiency.

In addition, sham arm will cross over to Felix arm at 90 days and go through step 10 in 9.3.1 and step 5 in 9.3.3.

All subjects will be encouraged to participate in the continued access phase where they will be followed up to 1 year.

9.3.9 In-Clinic/Virtual Visit at 180 Days (V6/±30 days)

There is a ±30 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic/virtual visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
    a) TETRAS Performance Subscale (items 6 and 7), as detailed in Section 9.3.1
2. Subject-rated assessments:
    a) TETRAS ADL items, as detailed in Section 9.3.1

b) Patient Global Impression of Severity (PGI-S)
c) Patient Global Impression of Improvement (PGI-I)
d) Survey of satisfaction and durability of effect;

3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V6;
5. Adverse Event;
6. Device Deficiency.

9.3.10 In-Clinic Visit at 1 year (V7/±30 days)

There is a ±30 days window to allow for flexibility in scheduling for this visit. During the follow-up in-clinic visit, the following will be assessed (while wearing the Felix device that's powered on with closed-loop stimulation on), tremor assessments will be measured after at least 40-min of closed-loop stimulation. All information will be analyzed and recorded into CRFs by the investigators.

1. Physician-rated assessments:
   a) TETRAS Performance Subscale (items1, 4, 6, 7 and 8), as detailed in Section 9.3.1
   b) Clinical Global Impression of Severity (CGI-S)
   c) Clinical Global Impression of Improvement (CGI-I)
2. Subject-rated assessments:
   a) TETRAS ADL items, as detailed in Section 9.3.1
   b) Patient Global Impression of Severity (PGI-S)
   c) Patient Global Impression of Improvement (PGI-I)
   d) Quality of Life in Essential Tremor Questionnaire (QUEST)
   e) Survey of satisfaction and durability of effect;
3. Medication: the drugs taken to treat tremor and concomitant medications for AEs and SAEs will be recorded;
4. Alcohol/marijuana consumption: record the alcohol/marijuana consumption the day before V7;
5. Adverse Event;
6. Device Deficiency.

9.4 Measures to control bias

In order to reduce bias, the following actions will be taken in this Study:

Training of investigators: Before the clinical trial is started, the investigators will be trained on the clinical trial protocol so that they can understand and be familiar with the investigational product and master all new information about the investigational product possible to be discovered during the implementation of the clinical trial.

Data management and data review: Data review will be conducted after the clinical trial is completed and before the database is locked, and relevant queries will be addressed in time to ensure the integrity and accuracy of the data.

Monitoring of the clinical trial: A monitoring plan will be prepared. The CRO designated by the Sponsor will appoint a CRA to perform regular field monitoring visits to the clinical investigational sites to ensure that all contents in the clinical trial protocol are strictly followed, and to check the raw materials to ensure their consistency with the contents in the eCRFs.

Audit of the clinical trial: A third party or the Sponsor will independently carry out audits by performing regular field audit visits to the clinical investigational sites to ensure that the CRA monitors the clinical trial according to the monitoring schedule, that all contents in the clinical trial protocol are strictly followed by random inspection, and that the raw materials are consistent with the contents in the eCRFs.

Improvement of the compliance of subjects: When talking about the informed consent with subjects, the investigators will explain the detailed procedures, purpose and significance of the study in a language that the subjects can understand to enhance their understanding and cooperation in the clinical trial process.

10. STATISTICAL CONSIDERATIONS

The statistical analysis planned for the clinical trial will be outlined in this Section. Detailed statistical analysis methods will be fully described in the Statistical Analysis Plan (SAP) and finalized prior to the completion of the primary effectiveness endpoint data collection.

10.1 Previous Clinical Study

Fasikl has conducted a pilot study of the Felix device in both the US (NCT05842434) and China under the same protocol. This is a prospective, open-label, multi-center, and multi-region pilot study designed to evaluate the safety and effectiveness of the Felix device. All subjects were followed for 7 days (with continuous at home treatment). Between June and September 2023, 12 ET patients were enrolled (7 in the US and 5 in China). The average patient age was 66 (range 42 to 87). There were 4 male patients and 8 female patients. 67% of patients had a family history of ET and 58% were on ET medication. Based on baseline TETRAS ratings, 33% of patients had mild tremor, 58% had moderate tremor, and 8% had severe tremor.

[redacted]

10.2 Power and Sample Size

The treatment effect is calculated as the average of the paired difference in the mADL scores between 90-day follow-up (f/u) and baseline pre-stimulation. The lower the value of the

difference, the higher the treatment effect. Denote the treatment effect for the Felix arm and the sham arm by D_{Felix} and D_{Sham}, respectively.

D_{Felix} = Mean of (mADL at 90-day f/u – mADL at baseline pre-stimulation) of the Felix arm

D_{Sham} = Mean of (mADL at 90-day f/u – mADL at baseline pre-stimulation) of the sham arm

The statistical hypothesis are defined as:

$$H0: D_{Felix} \geq D_{Sham}$$

$$H1: D_{Felix} < D_{Sham}$$

Assumptions:

- 2:1 randomization between Felix and sham
- [redacted]
- One-sided alpha of 0.025

Using t-test for two independent samples with equal variances, a total sample size of 120 will provide 92% power.

Test of equal variance will be performed and if the variances are significantly different, then t-test for two independent samples with unequal variances will be used instead. Details will be specified in the SAP.

10.3 Poolability

There is no evidence suggesting that race is a factor for ET. The use of the TETRAS assessments, which has "exceptional inter- and intra-rater reliabilities"[14], will ensure consistency in the study. All raters in the study will have to be certified by the tremor research group (TRG) who created the TETRAS assessments. Activities included in TETRAS ADL are common and relevant in everyday life among patients in both the US and China. The standard of care for ET is also similar between the two countries. A detailed description of the ET diagnosis, the patient populations, and the standard of care will be provided in a future submission.

Poolability of the primary endpoint will be tested. Baseline covariates will be compared to identify potential imbalances between patients from the two countries. Covariate-adjusted analysis may be conducted to adjust for these imbalances as well as geography. Details will be specified in the SAP.

10.4 Analysis Population

10.4.1 Intent to Treat (ITT)

The Intent to Treat (ITT) analysis set is defined as patients who have been randomized. In

accordance with the ITT principle, subjects will be kept in their originally assigned treatment group.

10.4.2 Modified Intent to Treat (mITT)

It is the dataset that includes all the patients who have been randomized and have gone through at least 1 day of at-home treatment.

10.4.3 Per-Protocol Set (PPS)

It refers to a subset of the ITT subjects who complete the evaluation of primary performance endpoint without major protocol deviation affected the evaluation of primary performance endpoint.

The primary analysis of the primary endpoint will be based on the ITT population. The primary endpoint analysis will also be performed on the mITT and PPS populations as a sensitivity analysis. All secondary efficacy endpoints will be analyzed for ITT, mITT, and PPS populations. The safety assessments will be analyzed for ITT population.

10.5 Study Success

Study success will be based on the primary analysis of the primary endpoint. Superiority of the Felix group compared to the Sham stimulation group will be assessed using the two-sided 95% confidence level of the difference of the average of the paired difference in the mADL scores between 90-day follow-up (f/u) and baseline pre-stimulation in two groups. The null hypothesis will be rejected if $p<0.025$ using t-test for two independent samples.

10.6 Subgroup Analysis

Subgroup analysis will be performed for potentially clinically important subgroups such as gender, tremor severity, tremor medication use, etc. Details will be specified in the SAP.

10.7 Missing Data

All primary analysis will be based on complete data. Sensitivity analysis of the primary endpoint will be performed using the imputation method detailed in the SAP.

10.8 Blinding

All randomized patients will be blinded to the treatment assignment until they have reached the primary endpoint (90 days). All raters will be blinded to the treatment assignment. It is impossible to blind site personnel who will perform device fitting because of the different internal mechanisms between Felix and the sham device. Training on the importance of maintaining blinding will be provided to all site personnel. A blinding assessment will be performed at the end of the randomized phase (90-day visit). Patients will be asked to guess which treatment arm they were assigned to, which will be compared to the actual assignment.

Statistical analysis will be performed by the statistical team at [redacted], who will be blinded to treatment assignment until the primary endpoint is reached. Sponsor personnel, with the

exception of the product support team, will be blinded to treatment assignment. A firewall will be established between the product support team and the rest of the sponsor personnel in order to ensure blinding.

10.9 Randomization

Randomization will be performed in the Interactive Response Technology (IRT) system via the randomization module of the system. Random codes will be generated using stratified blocked randomization by SAS 9.4. Stratification factors include:

- [redacted]
- [redacted]

Randomization will be managed directly by the eCRF platform.

All eligible subjects enrolled in the study will be followed for 90 days with the option to continue up to 1 year. Subjects will be randomly assigned in a 2:1 allocation ratio to either the Felix group or Sham Stimulation group.

10.10 Reject Criteria of Subjects

Before statistical analysis of data, the principal investigator, Sponsor, and statistician should identify whether any of the following situations occurs for subject, and the principal investigator should comprehensively identify whether to reject the subjects according to factors such as the degree of completion of the clinical trial and the reason for rejection and give relevant explanations. Any subject in the ITT population having any of the following conditions may be considered not be included in the PPS:

1) Subjects who are selected not according to the inclusion/exclusion criteria;
2) Subjects whose participation in the clinical trial is terminated by the investigators due to other factors based on the investigator's judgement;
3) Subjects who do not comply with the clinical trial protocol with poor compliance during the clinical trial.

The subjects to be rejected will be discussed and determined by the investigators, the Sponsor, data managers and statisticians on the data review meeting.

10.11 Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation at any time or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated serious adverse device effect (USADE) occurs and it presents an unreasonable risk to the participating subjects
- Further product development is cancelled

Should the Sponsor discontinue the clinical investigation, sites will follow subjects per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance reporting requirements. The investigator shall return all clinical investigation materials (including devices) to the Sponsor and provide a written statement to the IRB (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in Section 12.5 of the CIP.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations created by the CIP and existing agreements for following the subjects enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, as indicated.

A Principal Investigator, IRB, or regulatory authority may also suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

11. MONITORING PLAN

Please see the Monitoring Plan for details.

12. DATA MANAGEMENT

[redacted] will be responsible for data management in this Study. The eCRF will be used for data collection in this Study. To ensure the completeness, accuracy, authenticity and reliability of the electronic data in the clinical trial, data management will be implemented in accordance with the requirements specified in applicable local laws.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

12.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a ‘need to know’ basis, including periodic review of access rights, and revocation of access when an individual’s employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to enter only pseudonymous Personal Information (key-coded) necessary to conduct the clinical investigation, such as the patient’s

medical condition, treatment, dates of treatment, etc., into Sponsor's data management systems. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device use or procedures, monitoring and quality control purposes. All parties will observe confidentiality of Personal Information always throughout the clinical investigation. All reports and data publications will preserve the privacy of each subject and confidentiality of his/her information.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and in storage.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

12.2 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. To comply with these regulatory requirements/GCP, sites should include the following information in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number, and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- AEs reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, electrocardiograms (ECGs), and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- Notes regarding CIP-required and prescription medications taken during the clinical investigation (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures will be completed by the patient electronically. The electronic CRF output will serve as source documentation.

12.3 Case Report Form Completion

Site research personnel trained on the CIP and CRF completion will perform the primary data

collection clearly and accurately based on source-documented hospital and/or clinic chart reviews. The investigator will ensure accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Sites will collect data on all subjects enrolled into the clinical investigation. Only authorized site personnel will be permitted to enter the CRF data through the electronic data capture (EDC) system deployed by the Sponsor. The Sponsor will use an electronic audit trail to track any subsequent changes of the entered data.

12.4 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

12.5 Investigational Devices Accountability

The Sponsor ships investigational products only to the Principal Investigator (the responsible leader of the investigational site) or his/her legal designee of each site, after sites receive documentation of site activation and shipping authorization is complete.

The Investigator or an authorized designee must maintain adequate records of the receipt and disposition of each investigational device, including part number, batch/lot number, and serial number (if applicable), date used, subject identification, and treating physician.

Storage locations for the devices at investigational sites must be locked with access restricted only to investigators and authorized personnel.

Sites must return all investigational devices associated with a device failure or device deficiency immediately to the Sponsor.

13. RISK AND BENEFIT ANALYSIS

13.1 Anticipated Clinical Benefits

The Felix system is expected to provide the following clinical benefits:

- Improvement of upper limb tremor.
- Improvement of quality of life (QoL).

Note that these benefits may be temporary and may diminish after completion of or withdrawal from this study.

13.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

During stimulation, patients may temporarily experience the following:

- **Discomfort with stimulation (e.g. stinging pain, electric tingling sensation, pain on skin, soreness, weakness, etc.).**
- **Skin irritation (e.g., redness, itchy skin, dry skin, rashes, electrical stimulation burns, etc.)**

- **Skin discoloration.**
- **Muscle contraction.**
- **Worsening of tremor.**

All of these are expected to resolve without intervention after readjusting the device, decreasing stimulation amplitude, or discontinuing stimulation.

For patients with unilateral stimulation, in the event of skin irritation, the device can be worn on the other wrist (following Step 10 of Section 9.3.1) until the skin irritation resolves.

13.3 Nonsignificant Risk Medical Device

Based on US FDA's "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors on Significant Risk and Nonsignificant Risk Medical Device Studies.", Fasikl Incorporated (the sponsor) has determined that this study is a nonsignificant risk medical device study (21 Code of Federal Regulations (CFR) 812.2(b)(1)(ii)).

13.4 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions, and instructions regarding patient selection, device fitting, device operation are included in the IFU.

Risks associated with the use of the device under investigation are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements, study monitoring to ensure adherence to the protocol. Sites will report all adverse events and device deficiencies to the Sponsor and the Sponsor will monitor internally for safety surveillance purposes.

14. QUALITY CONTROL AND QUALITY ASSURANCE

14.1 CIP Amendments

The Sponsor will provide approved CIP amendments to the Investigators prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB’s approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Sites must document in writing acknowledgement/approval of the CIP amendment by the IRB prior to implementation of the CIP amendment. Sites must also provide copies of this documentation to the Sponsor.

14.2 Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, investigational device usage, electronic case report form completion, and clinical investigation

personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training.

14.3 Monitoring

Sponsor and the study principal investigator will monitor the clinical investigation over its duration.

14.4 Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety, and well-being of the subject, or to eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing within 5 working days.

Except in such an emergency, prior approval by the Sponsor is required for changes in or deviations from the CIP.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP, or any other conditions of the clinical investigation may result in further escalation, including securing compliance or, at its sole discretion, the Sponsor may terminate the investigator's participation in the clinical investigation.

15. ETHICAL ISSUES AND INFORMED CONSENT IN THE CLINICAL TRIAL

15.1 Ethical considerations

The Principal Investigator at each investigational site will obtain IRB approval for the CIP and ICF/other written information provided to the patient prior to consenting and enrolling patients in this clinical investigation. The site must receive the approval letter prior to the start of this clinical investigation and provide a copy to the Sponsor.

Sites will submit any amendments to the CIP as well as associated ICF changes to the IRB and written approval obtained prior to implementation, according to each institution's IRB requirements.

No changes will be made to the CIP or ICF or other written information provided to the patient without appropriate approvals, including IRB, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB of the progress of this clinical investigation, per IRB requirements. Written approval must be obtained

from the IRB yearly to continue the clinical investigation, or according to each institution's IRB requirements.

Sites will not perform any investigative procedures, other than those defined in this CIP, on the enrolled subjects without the written agreement of the IRB and the Sponsor.

15.2 Informed consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB. This process will include a verbal discussion with the patient on all aspects of the clinical investigation that are relevant to the patient's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Sites must inform patients about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty, or loss of benefits to which the patient is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the patient and will respect patient's legal rights. Financial incentives will not be given to patients. Patients may be compensated for time and travel directly related to the participation in the clinical investigation. The site shall provide the patient with the Informed Consent form written in a language that is understandable to the patient and that has been approved by the center's IRB. The patient shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the patient understands the information provided. If the patient agrees to participate, they must sign and date the Informed Consent form, along with the person obtaining the consent prior to any clinical investigation-specific procedures. The site will file the signed original in the patient's hospital or research charts, and provide a copy to the patient.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, sites will ask the subject to confirm their continuing informed consent in writing.

A template informed consent form (ICF) will be provided under a separate cover. Refer to the ICF and CIP procedure for guidance on managing the content.

15.2.1 Special Circumstances for Informed Consent

This clinical investigation excludes the following individuals from participation:

- Individuals unable to make the decision to participate in a clinical investigation on their own or who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.

- Individuals under the age of 18 or age of legal consent from the clinical investigation population.
- Individuals unable to read or write.
- Pregnant or breastfeeding women.

In addition, sites must obtain an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and China GCP, from the subject.

16. ADVERSE EVENT

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

16.1 Definition

16.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

As part of ISO14155 Section 3.2, the Adverse Event definition has the following notes:

Note 1: This definition includes events related to the medical device under investigation or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

16.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,

b) Led to a serious deterioration in health of the subject, users, or other persons as defined by one or more of the following:

   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function, or
   3. in-patient hospitalization or prolongation of existing hospitalization, or
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
   5. chronic disease

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for a pre-existing condition, or a procedure required by the CIP without a serious deterioration in health, is not considered to be an SAE.

16.1.3 Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use errors and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

16.1.4 Adverse Device Effect (ADE)

An Adverse Device Effect (ADE) is an AE related to the use of an investigational medical device. This definition includes AEs resulting from insufficient or inadequate Instructions for Use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. The definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

16.1.5 Unanticipated Serious Adverse Device Effect (USADE) / Unanticipated adverse device effect (UADE)

Unanticipated (serious) adverse device effect (UADE/USADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

16.2 Assessment of Severity

The course, severity, treatment and regression of each AE should be observed in a detailed way and recorded into the AE report form. The severity of AEs can be graded as mild, moderate or severe according to the following criteira.

1) Mild: Event, signs, or symptoms that do not interfere with the subject's daily activity, are usually considered self-limiting, can be treated with non-prescription type medications, and do not require medical intervention.

2) Moderate: Event may interfere or cause low level inconvenience with the subject's daily activity. Requires medical intervention and/or treatment; however, unlikely to require hospitalization or be considered potentially life-threatening in nature.

3) Severe: Event may cause significant discomfort to the subject and/or interferes with the subject's daily activity. Requires medical intervention and/or treatment to preclude a permanent impairment; may be life threatening and/or require hospitalization.

16.3 Device relationship

Relevance between an AE and the investigational medical device used can be identified as related, likely related, unlikely related or not related as described below:

Related to the investigational medical device: (1) there is a reasonable temporal relationship between the two; (2) the risks from the investigational medical device are known or can be explained by the mechanism of the investigational medical device; (3) the injury decreases or disappears after stopping using the investigational medical device; (4) the injury reappears after reusing the investigational medical device; and (5) it cannot be explained by other influencing factors. The AE should be identified as "**related**" to the investigational medical device when all the five criteria mentioned above are met, or "**likely related**" to the investigational medical device when any two of the five criteria mentioned above are met.

Not related to the investigational medical device: (1) there is no reasonable temporal relationship between the two; (2) the AE is impossible to be caused by the investigational medical device; and (3) the AE can be explained by the concomitant devices/medications, the progression of the patient's disease, or the impacts of other treatments. The AE should be identified as "**not related**" to the investigational medical device when all the three criteria mentioned above are met, or "**unlikely related**" to the investigational medical device when any one of the three criteria mentioned above is met.

16.4 Adverse Event and Device Deficiency/Device Malfunction Reporting

16.4.1 Adverse Event Reporting

Report the Adverse Event will be done according to local regulation.

Safety surveillance and reporting starts as soon as the patient is beginning the stimulation in the clinical investigation. Adverse events will not be collected for screen failure subjects. Safety surveillance and reporting will continue until sites perform the last follow-up visit, the subject is deceased, the subject concludes participation in the clinical investigation, or the subject withdraws from the clinical investigation. Sites will collect all adverse event data, including deaths and device deficiency data (if applicable), throughout the period defined above and will report these events to the Sponsor on a CRF. Sites should update additional information regarding an adverse event on the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

Full details of the event, treatment, and an initial assessment of the relationship between the investigational device will be provided in the report. The report shall be prepared by the principal investigator.

Serious Adverse Event Reporting (if applicable)

All SAEs must be reported to the Sponsor or delegate immediately or within 24 hours of Site Study Team becoming aware of the event being defined as serious.

Sites must record the date the site staff became aware that the event met the criteria of an SAE in the source document. The Investigator will further report the SAE to the local IRB according to the institution's IRB reporting requirements.

The sponsor shall, within 7 days after receiving the information of death or life-threatening SAEs related to the medical device, and within 15 days after receiving the information of non-death or non-life-threatening SAEs related to the medical device and other serious safety risks, report to the other clinical sites of medical devices involved in this clinical trials, ethics committees and principal investigators. Report to the relevant regulators and take risk control measures; If there is any information that may affect the safety of the subjects, the implementation of clinical trials on medical devices, or the consent of the Ethics Committee, it shall promptly organize the amendment of the clinical trial protocol, informed consent, other information provided to the subjects, and other relevant documents, and submit it to the Ethics Committee for review.

Unanticipated Adverse Device Effect Reporting (if applicable)

The Sponsor requires the Investigator to report any USADE/UADE to the Sponsor as soon as possible but no later than 10 working days of the investigator's knowledge of the event, unless local requirements are more stringent, and to the IRB per IRB requirements.

The sponsor who conducts an evaluation of an unanticipated adverse device effect shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

16.4.2 Device Deficiency/Malfunction Reporting

Sites should report all device deficiencies/malfunctions on the appropriate CRF form. Report the Device Deficiency/Malfunction will be done according to local regulation.

The investigator must report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than 10 working days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

Sites must report device deficiencies/malfunctions to the IRB per the investigative site's local requirements.

Sites should return the device to the Sponsor.

Issues related to the patient's smartphone that is unrelated to the study device or its corresponding App are not considered as device deficiency/malfunction.

17. DIRECT ACCESS TO SOURCE DATA AND DOCUMENTS

The investigator/institution will permit direct access to source data/documents for performing clinical investigation-related monitoring, audits, IRB review and regulatory inspections.

The access and editing permissions for other source data are detailed in the SOPs of corresponding departments in accordance with the requirements specified in applicable local laws and regulations and technical specifications.

Subjects providing informed consent are agreeing to allow clinical investigation monitors or regulatory authorities, including foreign countries, to review in confidence any records identifying the subjects in this clinical investigation. This information may be shared with regulatory agencies; however, the Sponsor undertakes not to otherwise release the subject's personal and private information.

18. INSURANCE

Patients who participate in this study will be insured for study related injuries according to local regulatory requirements. Hangzhou Fasikl Technology Co., LTD and Fasikl Incorporated will organize appropriate insurance coverage which will be available throughout the entire study.

19. PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. The Sponsor must review and approve any proposals for publications or presentations by the investigators in a timely manner in compliance with the Sponsor’s publication policy set forth in the Clinical Trial Agreement. The sponsor will cooperate with the PI in developing a manuscript reporting the results of this trial in a timely fashion. Sponsor agrees that publication of the results will occur regardless of the outcome of the study.

The Sponsor will be responsible for determining whether to register the clinical investigation on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event the Sponsor determines that the clinical investigation should be registered, the Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation.

20. RESPONSIBILITIES OF EACH PARTY

Sites, investigator and sponsor will perform their respective responsibilities in accordance with local regulations.

21. SUMMARY OF THE REVISION HISTORY IN THE CASE OF AMENDMENTS

[redacted]			
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

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Appendix 1: TRG ESSENTIAL TREMOR RATING ASSESSMENT SCALE (TETRAS©) V 3.1[1]

TETRAS mADL score is a composite sum of items 2 to 11 of the TETRAS ADL subscale and items 6 (bilateral) and 7 (dominant hand) of the TETRAS Performance subscale. TETRAS mADL score is calculated as the sum of all 12 items and ranges from 0 to 52.

Activities of Daily Living Subscale

Rate tremor's impact on activities of daily living (0 - 4 scoring).

1. Speaking

Score	Grade	Result of score
0	Normal.	
1	Slight voice tremulousness, only when "nervous".	
2	Mild voice tremor. All words easily understood.	
3	Moderate voice tremor. Some words difficult to understand.	
4	Severe voice tremor. Most words difficult to understand.	

2. Feeding with a spoon

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with feeding with a spoon.	
2	Mildly abnormal. Spills a little.	
3	Moderately abnormal. Spills a lot or changes strategy to complete task such as using two hands or leaning over.	
4	Severely abnormal. Cannot feed with a spoon.	

3. Drinking from a glass

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with drinking from a glass.	
2	Mildly abnormal. Spills a little.	

[1] Elble R, et al., Reliability of a new scale for essential tremor, Mov Disord. 2012; 27(12):1567-1569.

3	Moderately abnormal. Spills a lot or changes strategy to complete task such as using two hands or leaning over.	
4	Severely abnormal. Cannot drink from a glass or uses straw or sippy cup.	

4. Hygiene

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with hygiene.	
2	Mildly abnormal. Some difficulty but can complete task.	
3	Moderately abnormal. Unable to do most fine tasks such as putting on lipstick or shaving unless changes strategy such as using two hands or using the less affected hand.	
4	Severely abnormal. Cannot complete hygiene activities independently.	

5. Dressing

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with dressing.	
2	Mildly abnormal. Able to do everything but has difficulty due to tremor.	
3	Moderately abnormal. Unable to do most dressing unless uses strategy such as using Velcro, buttoning shirt before putting it on or avoiding shoes with laces.	
4	Severely abnormal. Cannot dress independently.	

6. Pouring

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with pouring.	
2	Mildly abnormal. Must be very careful to avoid spilling but may spill occasionally.	
3	Moderately abnormal. Must use two hands or uses other strategies to avoid spilling.	
4	Severely abnormal. Cannot pour.	

7. Carrying food trays, plates or similar items

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not interfere with carrying food trays, plates or similar items.	
2	Mildly abnormal. Must be very careful to avoid spilling items on food tray.	
3	Moderately abnormal. Uses strategies such as holding tightly against body to carry.	
4	Severely abnormal. Cannot carry food trays or similar items.	

8. Using Keys

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but can insert key with one hand without difficulty.	
2	Mildly abnormal. Commonly misses target but still routinely puts key in lock with one hand.	
3	Moderately abnormal. Needs to use two hands or other strategies to put key in lock.	
4	Severely abnormal. Cannot put key in lock.	

9. Writing

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor present but does not interfere with writing.	
2	Mildly abnormal. Difficulty writing due to the tremor.	
3	Moderately abnormal. Cannot write without using strategies such as holding the writing hand with the other hand, holding pen differently or using large pen.	
4	Severely abnormal. Cannot write.	

10. Working. If patient is retired, ask as if they were still working. If the patient is a housewife, ask the question as it relates to housework:

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor is present but does not affect performance at work or at home.	
2	Mildly abnormal. Tremor interferes with work; able to do everything, but with errors.	

3	Moderately abnormal. Unable to continue working without using strategies such as changing jobs or using special equipment.	
4	Severely abnormal. Cannot perform any job or household work.	

11. Overall disability with the most affected task (Name task, e.g. using computer mouse, writing, etc.)

Note: The tasks evaluated in each follow-up period should be consistent with tasks selected in Pre-Stimulation Assessments (V1).

Task _____

Score	Grade	Result of score
0	Normal.	
1	Slightly abnormal. Tremor present but does not affect task.	
2	Mildly abnormal. Tremor interferes with task but is still able to perform task.	
3	Moderately abnormal. Can do task but must use strategies.	
4	Severely abnormal. Cannot do the task.	

12. Social Impact

Score	Grade	Result of score
0	None.	
1	Aware of tremor, but it does not affect lifestyle or professional life.	
2	Feels embarrassed by tremor in some social situations or professional meetings.	
3	Avoids participating in some social situations or professional meetings because of tremor.	
4	Avoids participating in most social situations or professional meetings because of tremor.	

Performance Subscale

Instructions

Scoring is 0 – 4. For most items, the scores are defined only by whole numbers, but 0.5 increments may be used if you believe the rating is between two whole number ratings and cannot be reconciled to a whole number. Each 0.5 increment in rating is specifically defined for the assessment of upper limb postural and kinetic tremor and the dot approximation task (items 4 and 8). All items of the examination, except standing tremor, are performed with the patient seated comfortably. For each item, score the highest amplitude seen at any point during the exam. Instruct patients not to attempt to suppress the tremor, but to let it come out.

1. Head tremor: The head is rotated fully left and right and then observed for 10s in mid position. Patient then is instructed to gaze fully to the left and then to the right with the head in mid position. The nose should be used as the landmark to assess and rate the largest amplitude excursions during the examination.

Score	Grade	Result of score
0	no tremor	
1	slight tremor (< 0.5 cm)	
2	mild tremor (0.5- < 2.5 cm)	
3	moderate tremor (2.5-5 cm)	
4	severe or disfiguring tremor (> 5 cm)	

4. Upper limb tremor: Tremor is assessed during three maneuvers: forward horizontal reach posture, lateral "wing beating" posture and finger-nose-finger testing. Each upper limb is assessed and scored individually. The forward horizontal reach posture is held for 10 seconds. The lateral wing beating posture is held for 20 seconds. The finger-nose-finger movement is executed three times. Amplitude assessment should be estimated using the maximally displaced point of the hand at the point of greatest displacement along any single plane. For example, the amplitude of a pure supination-pronation tremor, pivoting around the wrist would be assessed at either the thumb or fifth digit.

Task	Right	Left
Forward outstretched postural tremor: Subjects should bring their arms forward, slightly lateral to midline and parallel to the ground for 10 seconds. The wrist should also be straight and the fingers abducted so that they do not touch each other, but not forcefully.		
Lateral "wing beating" postural tremor: Subjects will abduct their arms parallel to the ground and flex the elbows so that the two hands do not quite touch each other and are at the level of the nose. The fingers are abducted so that they do not touch each other, but not forcefully. The posture should be held for 20 seconds.		
Kinetic tremor: Subjects extend only their index finger. They then touch a set object or the examiners finger located to the full extent of their reach, which is located at the same height		

(parallel to the ground) and slightly lateral to the midline. Subjects then touch their own nose (or chin if the tremor is severe) and repeat this back and forth three times. Only the position along the trajectory of greatest tremor amplitude is assessed. This will typically be either at the nose or at the point of full limb extension.		

For all three hand tremor ratings

Score	Grade
0	no tremor
1	tremor is barely visible
1.5	tremor is visible, but less than 1 cm
2	tremor is 1- < 3 cm amplitude
2.5	tremor is 3- < 5 cm amplitude
3	tremor is 5- < 10 cm amplitude
3.5	tremor is 10- < 20 cm amplitude
4	tremor is ≥ 20 cm amplitude

6. Archimedes spirals: Demonstrate how to draw Archimedes spiral that approximately fills ¼ of an unlined page of standard (letter) paper. The lines of the spiral should be approximately 1.3 cm (0.5 inch) apart. Then ask the subject to copy the spiral. Test and score each hand separately. Use a ballpoint pen. The pen should be held such that no part of the limb touches the table. Secure the paper on the table in a location that is suitable for the patient's style of drawing. Score the tremor in the spiral, not the movement of the limb.

Score	Grade	Right	Left
0	normal		
1	slight: tremor barely visible.		
1.5	/		
2	mild: obvious tremor		
2.5	/		
3	moderate: portions of figure not recognizable.		
3.5	/		
4	severe: figure not recognizable		

7. Handwriting: Have patient write the standard sentence "This is a sample of my best handwriting" using the dominant hand only. Patients must write cursively (i.e., no printing). They cannot hold or stabilize their hand with the other hand. Use a ballpoint pen. Secure the paper on the table in a

location that is suitable for the patient's style of writing. Score the tremor in the writing, not the movement of the limb.

Score	Grade	Result of score
0	normal	
1	slight: untidy due to tremor that is barely visible.	
1.5	/	
2	mild: legible, but with considerable tremor.	
2.5	/	
3	moderate: some words illegible.	
3.5	/	
4	severe: completely illegible	

8. Dot approximation task: The examiner makes a dot or X and instructs the subject to hold the tip of the pen "as close as possible to the dot (or center of an X) without touching it, (ideally approximately 1 mm) for 10 seconds". Each hand is scored separately.

Score	Grade	Right	Left
0	no tremor		
1	tremor is barely visible		
1.5	tremor is visible, but less than 1 cm		
2	tremor is 1- < 3 cm amplitude		
2.5	tremor is 3- < 5 cm amplitude		
3	tremor is 5- < 10 cm amplitude		
3.5	tremor is 10- < 20 cm amplitude		
4	tremor is $\geq$ 20 cm amplitude		

Appendix 2:

Clinical Global Impression of Severity (CGI-S)

Considering your total clinical experience with this particular population, how severe is the essential tremor in the patient at this time?

Score	Grade	Result of score
1	Normal, no tremor	
2	Borderline tremor	
3	Mild tremor	
4	Moderate tremor	
5	Marked tremor	
6	Severe tremor	
7	Among the most extreme tremor	

Clinical Global Impression of Improvement (CGI-I)

Compared to the patient's condition at admission to the project [prior to stimulation initiation], this patient's condition is:

Score	Grade	Result of score
1	Very much improved	
2	Much improved	
3	Minimally improved	
4	No change	
5	Minimally worse	
6	Much worse	
7	Very much worse	

Appendix 3:

Patient Global Impression of Severity (PGI-S)

Check the one number that best describes how your tremor condition is now.

Score	Grade	Result of score
1	Normal, no tremor	
2	Borderline tremor	
3	Mild tremor	
4	Moderate tremor	
5	Marked tremor	
6	Severe tremor	
7	Among the most extreme tremor	

Patient Global Impression of Improvement (PGI-I)

Check the one number that best describes how your tremor condition is now, compared with how it was before you began taking device stimulation in this study.

Score	Grade	Result of score
1	Very much improved	
2	Much improved	
3	Minimally improved	
4	No Change	
5	Minimally worse	
6	Much worse	
7	Very much worse	

Appendix 4: Quality of Life in Essential Tremor Questionnaire (QUEST)

Patient's Name: _____ID: _____Date: ____ / ____ / ____

Gender: Male Female Date of Birth: ____ / ____ / ____

Health Status

In general, how would you rate your overall health? (0=very poor health, 100=excellent/perfect health)

Circle: 0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Overall Quality of Life

Overall, how would you rate your quality of life? (0=very poor health, 100=excellent/perfect health)

Circle: 0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

General Information

In the past month, has your tremor interfered with your sexual satisfaction?

Y N

In the past month, have you had side effects from tremor medications?

Y N

In the past month, have you been satisfied with the tremor control achieved by your medications?

Y N

Which most appropriately describes your work status?

Never worked

Not working, retired because of tremor

Not working, retired NOT due to tremor

Working full time

Working part time

TREMOR SELF ASSESSMENT

For the purposes of this questionnaire, tremor is defined as uncontrollable shaking or quivering of the body part in question.

On a typical day, how many of your waking hours do you have tremor in ANY body part?

Circle: 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

Put a mark in the box to rate the severity of your tremor in each of the body parts listed below.

None - no tremor at any time

Mild - mild tremor not causing difficulty in performing any activities

Moderate - tremor causes difficulty in performing **some** activities

Marked - tremor causes difficulty in performing **most** or **all** activities

Severe - tremor **prevents** performing some activities

	None	Mild	Moderate	Marked	Severe
1. Head	□	□	□	□	□
2. Voice	□	□	□	□	□
3. Right arm/hand	□	□	□	□	□

4. Left arm/hand	☐	☐	☐	☐	☐
5. Right leg/foot	☐	☐	☐	☐	☐
6. Left leg/foot	☐	☐	☐	☐	☐

For each question below, please mark the box which best describes your current situation.

For example: N R S F A

N = Never/No

R = Rarely

S = Sometimes

F = Frequently

A = Always/Yes

NA = Not **A**pplicable

1. My tremor interferes with my ability to communicate with others. N R S F A
2. My tremor interferes with my ability to maintain conversations with others. N R S F A
3. It is difficult for others to understand my speech because of my tremor. N R S F A
4. My tremor interferes with my job or profession. NA N R S F A
5. I have had to change jobs because of my tremor. NA N R S F A
6. I had to retire or take early retirement because of my tremor. N [redacted] A
7. I am only working part time because of my tremor. NA N [redacted] A
8. I have had to use special aids or accommodations in order to continue my job due to my tremor. NA N R S F A
9. My tremor has led to financial problems or concerns. N R S F A
10. I have lost interest in my hobbies because of my tremor. N R S F A
11. I have quit some of my hobbies because of my tremor. N [redacted] A
12. I have had to change or develop new hobbies because of my tremor. N [redacted] A
13. My tremor interferes with my ability to write (for example, writing letters, completing forms). N R S F A
14. My tremor interferes with my ability to use a typewriter or computer. NA N R S F A
15. My tremor interferes with my ability to use the telephone (for example, dialing, holding the phone). N R S F A
16. My tremor interferes with my ability to fix small things around the house (for example, change light bulbs, minor plumbing, fixing household appliances, fixing broken items). N R S F A
17. My tremor interferes with dressing (for example, buttoning, zipping, tying shoes). N R S F A
18. My tremor interferes with brushing or flossing my teeth. N R S F A
19. My tremor interferes with eating (for example, bringing food to mouth, spilling). N R S F A
20. My tremor interferes with drinking liquids (for example, bringing to mouth, spilling, pouring). N R S F A
21. My tremor interferes with reading or holding reading material. N R S F A
22. My tremor interferes with my relationships with others (for example, my family, friends, coworkers). N R S F A
23. My tremor makes me feel negative about myself. N R S F A
24. I am embarrassed about my tremor. N R S F A

25. I am depressed because of my tremor. **N R S F A**
26. I feel isolated or lonely because of my tremor. **N R S F A**
27. I worry about the future due to my tremor. **N R S F A**
28. I am nervous or anxious. **N R S F A**
29. I use alcohol more frequently than I would like to because of my tremor. **N R S F A**
30. I have difficulty concentrating because of my tremor. **N R S F A**

If a question is Not Applicable, "X" through NA and leave blank--do not assign a score of 0.

Scoring algorithm:	*Total **applicable** points for dimension* / *Total possible points (# of **applicable** question x 4) for each dimension*	x 100=	dimension score

N=0 **R**=1 **S**=2 **F**=3 **A**=4 **NA=blank**

Note: Questions 6, 7, 11, & 12—0 **OR** 4 **points possible (if applicable)**

Appendix 5: Survey of satisfaction and durability of effect

Patient survey:

Q5-11 will be surveyed at **V2** (14±3 days);

Q12-14 will be surveyed at **V2** (14±3 days), **V5** (90±14 days) and **V7** (1 year±30 days);

Q1-4, Q15 will be surveyed at **V2** (14±3 days), **V3** (30±7 days), **V4** (60±7 days), **V5** (90±14 days), **V6** (180±30 days) and **V7** (1 year±30 days);

Q16 will be surveyed at **V5** (90±14 days) and **V7** (1 year±30 days);

Q17-Q18 will be surveyed at **V5** (90±14 days).

1. Overall, how satisfied are you with the treatment during the study?

Score	Grade	Result of score
1	Extremely satisfied	
2	Very satisfied	
3	Somewhat satisfied	
4	Neutral	
5	Somewhat unsatisfied	
6	Very unsatisfied	
7	Extremely unsatisfied	

2. Overall, how comfortable was the stimulation?

Score	Grade	Result of score
1	Extremely comfortable	
2	Very comfortable	
3	Somewhat comfortable	
4	Neutral	
5	Somewhat uncomfortable	
6	Very uncomfortable	
7	Extremely uncomfortable	

3. While being treated with the Felix device, were you able to satisfactorily perform the daily tasks that were mostly impacted by tremor?
   - ☐ Yes
   - ☐ No

4. How convenient is it to use the Felix system on a daily basis?

Score	Grade	Result of score
1	Extremely convenient	
2	Very convenient	
3	Somewhat convenient	
4	Neutral	
5	Somewhat inconvenient	
6	Very inconvenient	
7	Extremely inconvenient	

5. How simple is it to power on/off the Felix device?

Score	Grade	Result of score
1	Extremely easy	
2	Very easy	
3	Somewhat easy	
4	Neutral	
5	Somewhat difficult	
6	Very difficult	
7	Extremely difficult	

6. How simple was it to connect Felix device to the smartphone app?

Score	Grade	Result of score
1	Extremely easy	
2	Very easy	
3	Somewhat easy	
4	Neutral	
5	Somewhat difficult	
6	Very difficult	
7	Extremely difficult	

7. How simple was it to charge the Felix device?

Score	Grade	Result of score
1	Extremely easy	
2	Very easy	
3	Somewhat easy	
4	Neutral	
5	Somewhat difficult	
6	Very difficult	
7	Extremely difficult	

8. How simple is it to perform regular maintenance of the Felix device?

Score	Grade	Result of score
1	Extremely easy	
2	Very easy	
3	Somewhat easy	
4	Neutral	
5	Somewhat difficult	
6	Very difficult	
7	Extremely difficult	

9. Were the provided instructions clear and understandable?

Score	Grade	Result of score
1	Extremely clear	

2	Very clear	
3	Somewhat clear	
4	Neutral	
5	Somewhat unclear	
6	Very unclear	
7	Extremely unclear	

10. Did you find the smartphone app interface visually clear and well-organized?

Score	Grade	Result of score
1	Extremely clear	
2	Very clear	
3	Somewhat clear	
4	Neutral	
5	Somewhat unclear	
6	Very unclear	
7	Extremely unclear	

11. Have the materials provided by Fasikl offered you enough guidance for operating the Felix device? Is there any information you believe should be incorporated into the instruction manual?
    _____

12. What do you like the most about the Felix device?
    _____

13. What do you like the least about the Felix device?
    _____

14. What improvements would you suggest?
    _____

15. On average, how long did tremor relief last after the device was turned off. (Unit: hours)
    _____hours

16. Would you be interested in buying this device when it's approved by the FDA/NMPA
    - ☐ Yes
    - ☐ No
    - ☐ Maybe

17. Which treatment group do you think you were assigned to?
    - ☐ Felix group
    - ☐ Sham Stimulation group

18. For Q17, why do you think so?
    - ☐ Treatment effect of the device

☐ Lack of treatment effect of the device
☐ Someone told me
☐ Other, please specify: _____