Real-world evidence for symptomatic relief in essential tremor using transcutaneous afferent patterned stimulation therapy

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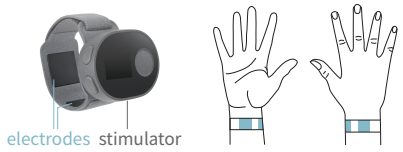
Background & Study Objective

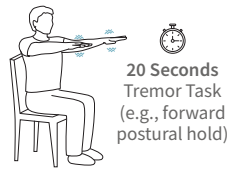
Essential tremor (ET) is one of the most common movement disorders in adults but has limited available treatment options. Transcutaneous afferent patterned stimulation (TAPS) is a wrist-worn, non-invasive neuromodulation therapy targeting the median and radial nerves with a bursting waveform individualized to each patient's tremor. TAPS has been shown to be a safe and effective symptomatic tremor relief therapy in single-session and extended-duration clinical studies[1-3], but how these results translate from a closely monitored clinical trial into a real-world setting is unknown. **This early post-market analysis evaluated the real-world efficacy and safety of TAPS therapy for symptomatic tremor relief in 44 ET patients over three months of non-supervised home use.**

Device Design & Calibration

Stimulator & electrodes



Device Calibration



The device consisted of a stimulator and detachable band containing two working electrodes positioned over the median and radial nerves and a counter- electrode positioned on the dorsum of the wrist.

The patient's tremor frequency was captured from a 20 second postural hold. The peak tremor frequency was determined onboard the device and used to tune a patient-specific stimulation pattern.

Therapy Prescription and Home Use

Device prescription and setup. Patients were prescribed a United States Food & Drug Administration-cleared TAPS therapeutic device (Cala Health, Burlingame, CA) following evaluation by a neurologist. Patients were given written instruction for setting up and calibrating the therapeutic device, with phone support available as needed. **Home use.** A therapy session consisted of 40 minutes of stimulation. Timing and frequency of device usage was at the discretion of each patient, though the therapy was labeled for symptomatic usage.

Patient consent: *Patients provided informed consent for their data to be included in this analysis. All device and survey data was de-identified prior to analysis.*

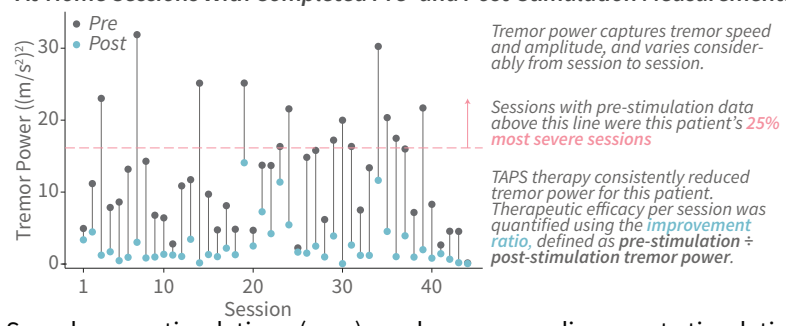
Disclosures: *SS, PC, AR, MG, and KR are current or former employees of Cala Health. RP and SI serve as clinical advisors for Cala Health.*

Tremor Motion Improvements

For the first 40 sessions and every 7th session thereafter, the device prompted patients to perform their tremor task before and immediately after stimulation. A triaxial accelerometer onboard the device measured tremor motion during this task. **Tremor severity was quantified using tremor power**, computed from the power spectral density of the accelerometer data.

Sample Tremor Motion Remote Measurements

At-Home Sessions With Completed Pre- and Post-Stimulation Measurements

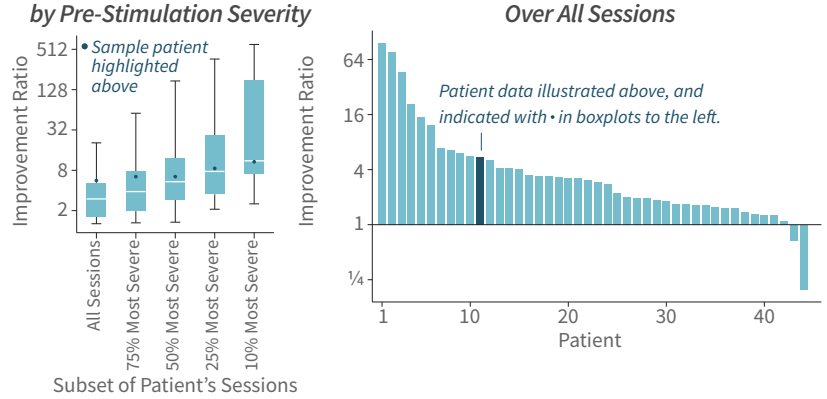


Sample pre-stimulation (grey) and corresponding post-stimulation (blue) tremor power measurements for a **representative patient (see below)**. Note, only sessions with completed pre- and post-stimulation measurements are illustrated; these sessions represent a subset of the total sessions completed by a patient over the analyzed 90-day period.

Symptomatic Tremor Improvement

Tremor Improvement by Pre-Stimulation Severity

Per-Patient Median Improvement Over All Sessions

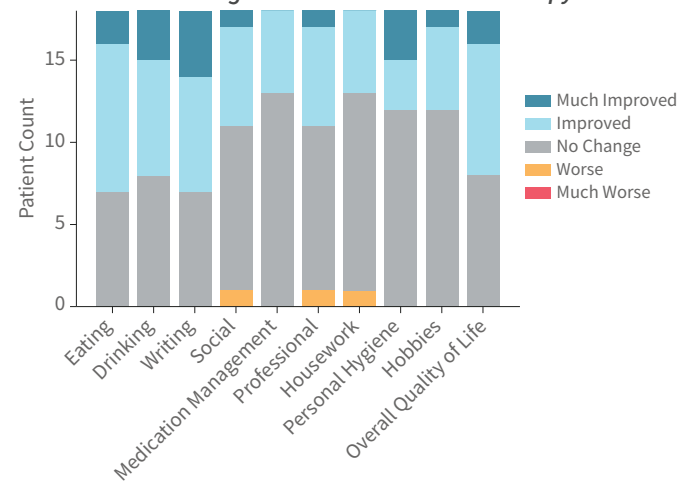


(Left) **Tremor reduction with therapy increased as a patient's tremor severity increased.** Whiskers represent 5th-95th percentile of data. (Right) Tremor power measurements from 1,751 therapy sessions showed that **93% of patients (41 of 44) had a ≥2-fold improvement (i.e., 50% reduction) in tremor power during their most severe sessions (i.e., when tremor relief was most needed)**, and **57% of patients had ≥2-fold improvement in tremor power over all sessions**.

Patient-Reported Outcomes

Following ninety days of device use, patients were sent an opt-in post-market survey. The survey asked patients to rate their tremor burden, preference for TAPS therapy relative to existing treatment options, areas where they would most like therapy to improve tremor symtoms, and improvement in tasks and quality of life with TAPS therapy.

Self-Rated Change In Activities With TAPS Therapy



18 of 44 patients completed the survey. Of these 18 patients, 61% reported having over 20 years of ET symptoms, and 83% reported having at least moderate tremor. Prior to trying TAPS, most (89%) patients had tried medication for tremor control, and 72% had tried two or more medications for tremor relief. With TAPS, **61% of patients (11 of 18) reported that eating, drinking, and/or writing improved and 56% of patients (10 of 18) reported that quality of life improved**. 9 of 18 patients preferred TAPS therapy to existing treatment options (medication or surgery).

Safety

3 of 44 patients reported minor adverse events (skin irritation or electrical burns) that resolved with temporary discontinuation of therapy and without medical intervention.

Conclusions

This early real-world evidence reinforces previous clinical trial findings on objective (kinematic) and patient-reported efficacy and safety of TAPS[3]. These results suggest that TAPS may be an attractive option for ET patients seeking symptomatic treatment with minimal side effects.

References:

[1] Lin PT et al. Noninvasive neuromodulation in essential tremor demonstrates relief in a sham-controlled pilot trial. Mov Disord 2018.

[2] Pahwa R et al. An Acute Randomized Controlled Trial of Noninvasive Peripheral Nerve Stimulation in Essential Tremor. Neuromod 2019.

[3] Isaacson S et al. Prospective home-use study on non-invasive neuromodulation therapy for essential tremor. Trem Hyperkin Mov 2020.