Paired Vagus Nerve Stimulation Therapy Using an External Stimulation Controller

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MicroTransponder

Presenters and Attendees

Gerard E. Francisco, MD

- The Wulfe Family Chair Of Physical Medicine And Rehabilitation
- Chairman And Professor (With Tenure), Distinguished Teaching Professor, UT Systems
- Chief Medical Officer And Clinical Scientist, TIRR Memorial Hermann
- Director, UTHealth NeuroRecovery Research Center At TIRR Memorial Hermann

Spencer Bailey, MBA, CPC

- VP Market Access and Reimbursement, MicroTransponder, Inc.

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- Market Access Manager, MicroTransponder, Inc.

Ischemic Stroke and Upper Limb Deficit: A Serious Problem

Acute Ischemic Stroke is treated in the hospital and the patient is referred for rehabilitation

Standard-of-Care Treatment = Rehabilitation

Inpatient Rehab and Step-Down

Acute Inpatient Rehab (IRF) | Subacute Rehab (SNF) | Long-Term Care Facility (LTCH)

Even after PT/OT 60% still have upper limb deficit

STOP

No other treatment options exist
Learn to live with disability

Upper limb deficit is a common and devastating outcome of ischemic stroke

- 40%-60% of stroke survivors have permanent and chronic upper limb deficit at 6 months[1]
- Most cannot drive, live independently or return to work – many become permanently and totally disabled[2]
- The burden on families, care-takers and society at large is significant, with post-acute care costs exceeding $96,000 in the first 3 years post-stroke[3,4]
- Each year, over 200,000 stroke survivors experience chronic upper limb deficit and have no other treatment alternatives

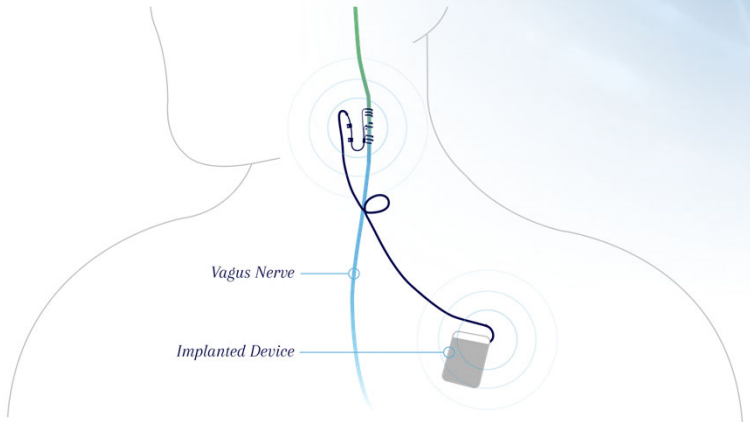
1. Pollock A, Baer G, Campbell P, et al. Physical rehabilitation approaches for the recovery of function and mobility following stroke. Cochrane Database Syst Rev. 2014 Apr 22;2014(4):CD001920.
2. Raghavan P. Upper Limb Motor Impairment After Stroke. Phys Med Rehabil Clin N Am. 2015;26(4):599-610.
3. Yousufuddin M, Moriarty JP, Lackore KA, et al. Initial and subsequent 3-year cost after hospitalization for first acute ischemic stroke and intracerebral hemorrhage. J Neurol Sci. 2020 Dec 15;419:117181.
4. Daras LC, Deutsch A, Ingber MJ, et al. Inpatient rehabilitation facilities' hospital readmission rates for Medicare beneficiaries treated following a stroke. Top Stroke Rehabil. 2021 Jan;28(1):61-71.

Vivistim® Paired Vagus Nerve Stimulation (VNS) Therapy

What is the Vivistim® System?

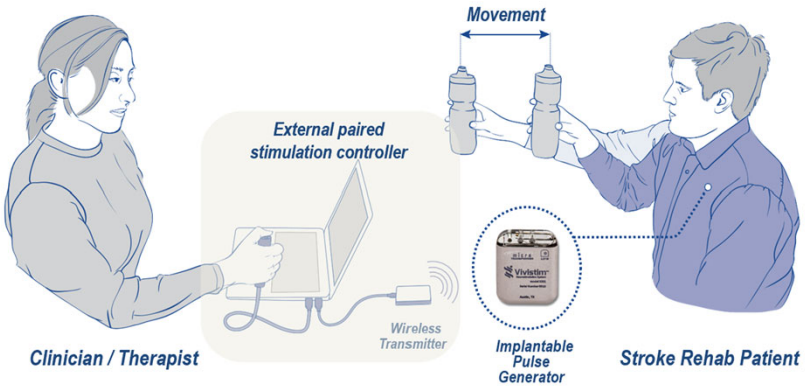
Vivistim® System is an implantable vagus nerve stimulator (VNS) generator and stimulation lead

- Insertion procedure performed in operating room and documented in the operative record (EHR)
- The generator (IPG) is placed in the chest through three small incisions, stimulation lead is placed on the vagus nerve during a 45 to 60-minute



Why is it called Paired VNS Therapy?

- The Vivistim System is “Paired” with movement to stimulate the development of new neural pathways
- The system is activated during in-clinic rehabilitation therapy by a therapist and at home by the patient during home therapy
- Pairing specific movements with vagus nerve stimulation is what delivers the clinical benefit



Vivistim® Paired VNS System

Implantable System

Vivistim® IPG
Model 1001 Implantable Pulse Generator (IPG)

Implantable Pulse Generator (IPG) similar in size, shape and external design to other implanted neurostimulators

Lead
Model 3000
Implantable Lead

Implantable lead similar to other vagus nerve leads
Available in both 2mm and 3mm cuff sizes

External Paired Stimulation Controller

Wireless Transmitter
Model 2000
Wireless Transmitter

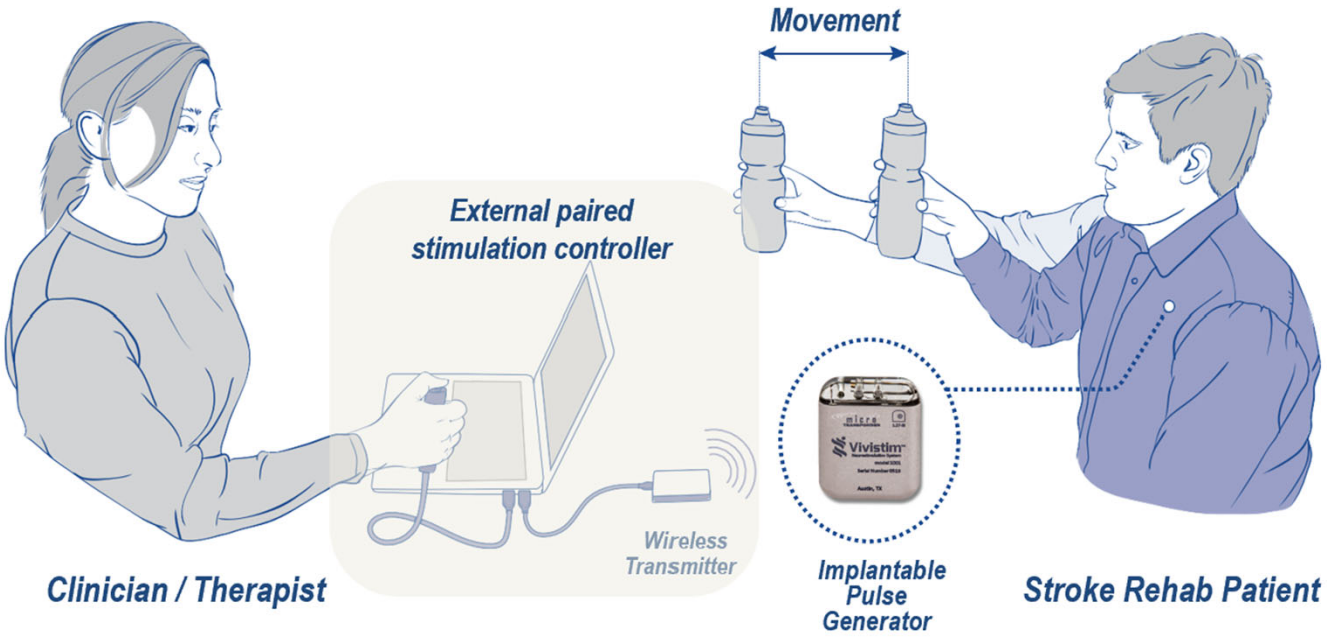
Bi-directional RF communication link between SAPS (Stroke Application and Programming Software) and the implanted IPG

SAPS Software and Laptop
Model 4001 Stroke Application & Programming Software

Therapist-controlled stimulation system that is used in in-clinic rehabilitation therapy and the interrogate and program the IPG

Vivistim® Paired Vagus Nerve Stimulation (VNS) Therapy

Indication for Use: The Vivistim® Paired VNS System intended to be used to stimulate the vagus nerve during rehabilitation therapy in order to reduce upper extremity motor deficits and improve motor function in chronic ischemic stroke patients with moderate to severe arm impairment.



Paired VNS Therapy

25-30 Hours of in-clinic Paired VNS rehabilitation therapy over 6-8 weeks

Home use includes 30-60 minutes per day, as directed by a therapist

Ongoing care management and periodic device checks

Overview of Vivistim® Published Clinical Studies

- Consistent results over three (3) crossover, sham controlled, randomized clinical study populations
  - **2-3X improvement** in arm and hand function over intensive rehab therapy alone
  - Significant impact on **QoL endpoints** (MAL, SIS, EQ5D, Beck Depression Index)
- Safety profile consistent with existing vagus nerve neurostimulator insertion procedures
- Paired VNS is effective up to 10 years post stroke

Publication Year	Study Type	Author	Title & Reference	Total Study Participants	AMA Level of Evidence	NCT Identifier
2021	Pivotal Trial	Dawson J, Liu CY, Francisco GE, Cramer SC, Wolf SL, Dixit A, Alexander J, Ali R, Brown BL, Feng W, DeMark L, Hochberg LR, Kautz SA, Majid A, O'Dell MW, Pierce D, Prudente CN, Redgrave J, Turner DL, Engineer ND, Kimberley TJ.	Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial. Lancet. 2021 Apr 24;397(10284):1545-1553.	108	1b	NCT03131960
2020	Pilot 1 Year Follow-up	Dawson J, Engineer ND, Prudente CN, Pierce D, Francisco G, Yozbatiran N, Tarver WB, Casavant R, Kline DK, Cramer SC, Van de Winckel A, Kimberley TJ.	Vagus Nerve Stimulation Paired With Upper-Limb Rehabilitation After Stroke: One-Year Follow-up Neurorehabil Neural Repair. 2020 Jul;34(7):609-615.	15	1b	NCT 02243020
2018	Pilot	Kimberley TJ, Pierce D, Prudente CN, Francisco GE, Yozbatiran N, Smith P, Tarver B, Engineer ND, Alexander Dickie D, Kline DK, Wigginton JG, Cramer SC, Dawson J.	Vagus Nerve Stimulation Paired With Upper Limb Rehabilitation After Chronic Stroke. Stroke. 2018 Nov;49(11):2789-2792.	17	1b	NCT 02243020
2016	Feasibility	Dawson J, Pierce D, Dixit A, Kimberley TJ, Robertson M, Tarver B, Hilmi O, McLean J, Forbes K, Kilgard MP, Rennaker RL, Cramer SC, Walters M, Engineer N.	Safety, Feasibility, and Efficacy of Vagus Nerve Stimulation Paired With Upper-Limb Rehabilitation After Ischemic Stroke. Stroke. 2016 Jan;47(1):143-50.	21	1b	NCT 01669161

Pivotal Trial Design and Primary/Secondary Endpoint Results

Study Design Overview

- 108 subjects assigned to either Intense Rehab with Paired VNS (treatment) or Intense Rehab with Sham VNS (Control)
- Crossover design, randomized, sham-controlled trial with triple-blinding across 15 clinical sites in the US and UK
- Average age of enrollment was 60.1 years old +/- 10
- The best practice, intense physical therapy was provided to both treatment and control groups

Endpoint/Measurement Tools

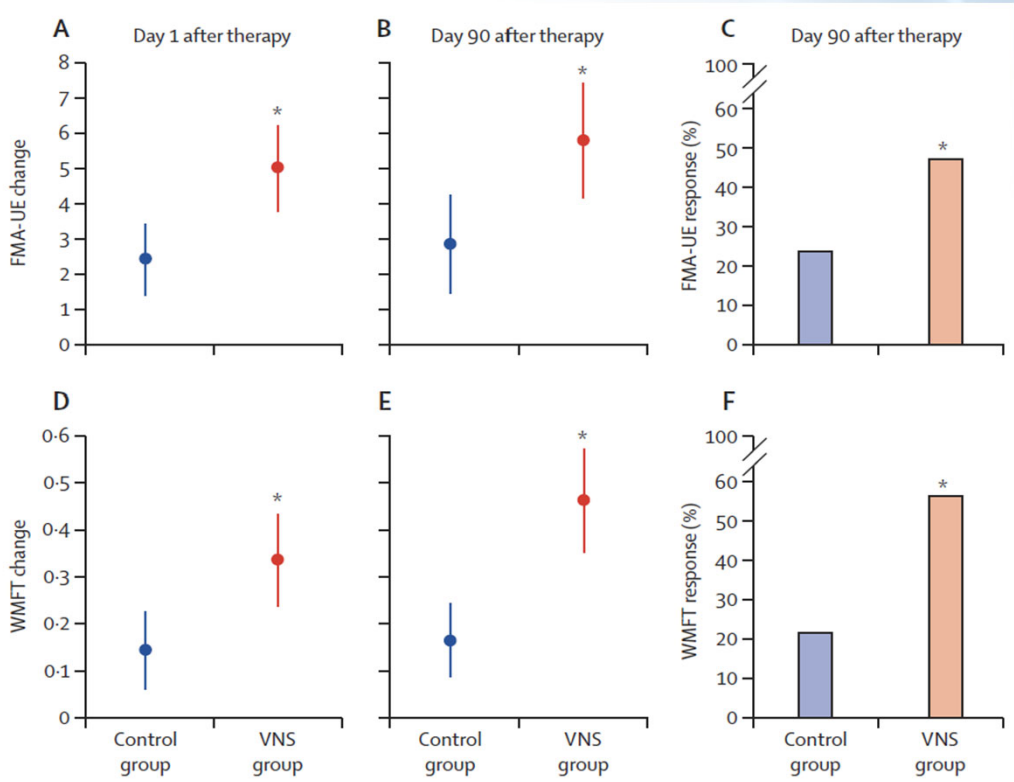
Primary Endpoint:

- *(FMA-UE) Upper Extremity Fugl-Meyer*
- Stroke-specific, performance-based impairment index

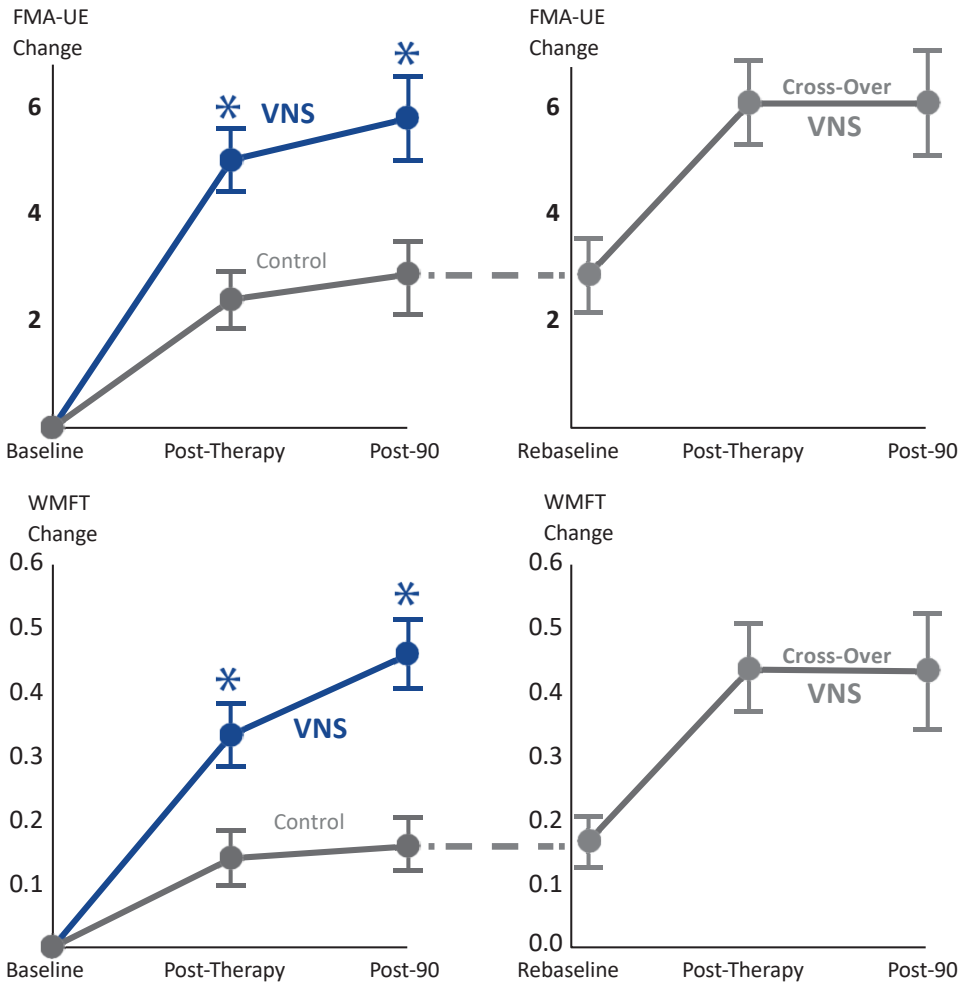
Secondary Endpoint:

- *(WMFT) Wolf Motor Function Test*
- Quantifies upper extremity (UE) motor ability through timed and functional tasks

Primary and Secondary Endpoint Results Day 1 and Day 90

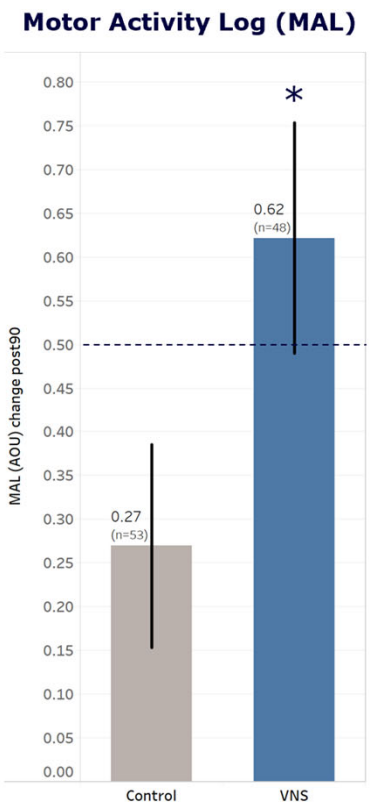


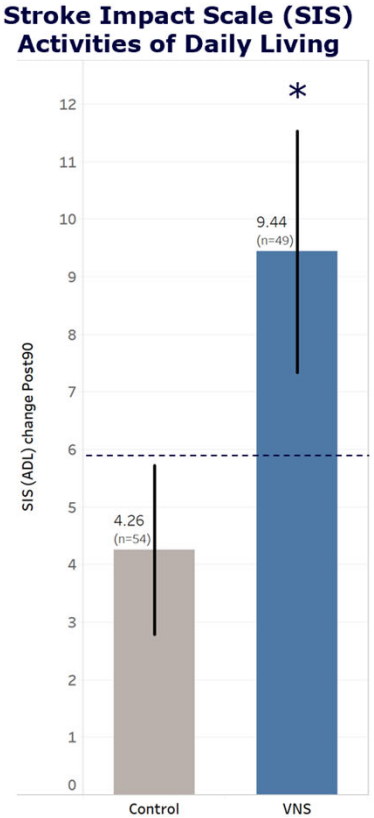
Vivistim® Paired VNS Therapy Crossover Outcomes

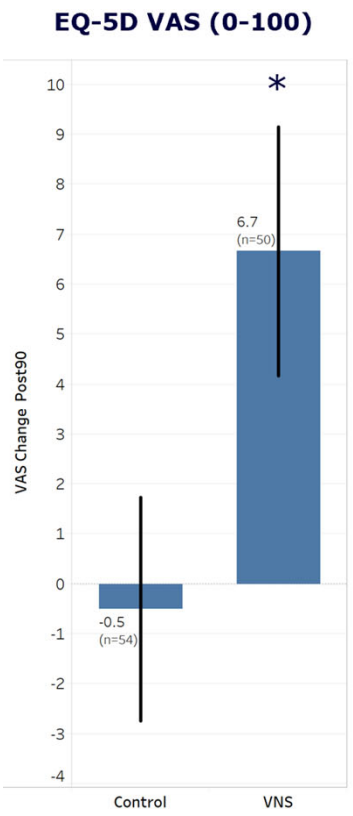


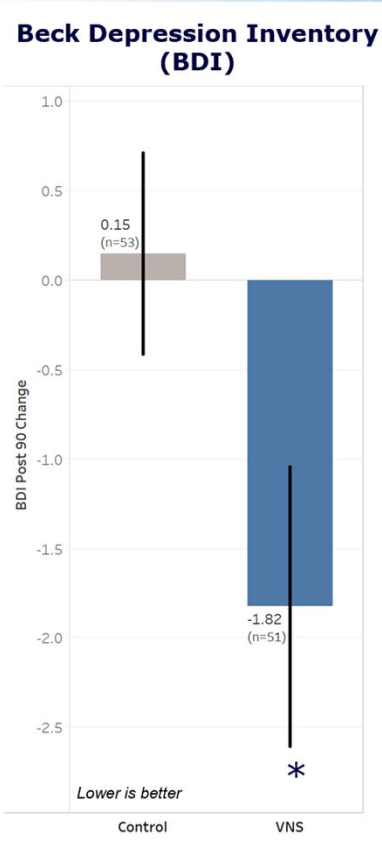
**Not all long-term data has not been monitored and data collection ongoing.*

Pivotal Trial - Activities of Daily Living and Quality of Life Measures









--- The generally accepted clinically meaningful cutoff for MAL is >= 0.5 for **chronic** stroke patients (Lang et al., 2008).

-------- The generally accepted clinically meaningful cutoff for SIS-ADL is >= 5.9 for **chronic** stroke patients (Lin et al., 2010).

* P <0.05

In Summary

Vivistim® is the only treatment option for chronic upper limb deficit as a result of a stroke

Vivistim® Paired VNS Therapy delivers better patient outcomes

- Shown to be effective from 6 months to 10 years post-stroke
- Consistent results across three (3) randomized controlled trials - 2-3X improvement in Wolf Motor Function Test (WMFT) and Fugl-Meyer Upper Extremity (FMA-UE) – which are the gold-standard in evaluating upper limb function
- Significant quality of life improvements – depression, function, return to activities of daily living
- Many patients reported being able to do many of the things they love again – gardening, driving, holding grandkids, housework

1. Dawson J, Liu CY, Francisco GE, et. al. Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial. Lancet. 2021 Apr 24;397(10284):1545-1553.