CLINICAL PROTOCOL

DULCET Study: A non-significant risk clinical investigation of the VibratoSleeve, a therapeutic ultrasound (TUS) phased array, for patients with ischemic and neuroischemic diabetic foot ulcers (DFU).

STUDY NO: S21-003 VER 2.3
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CONFIDENTIAL

STUDY SPONSOR

Vibrato Medical, Inc.

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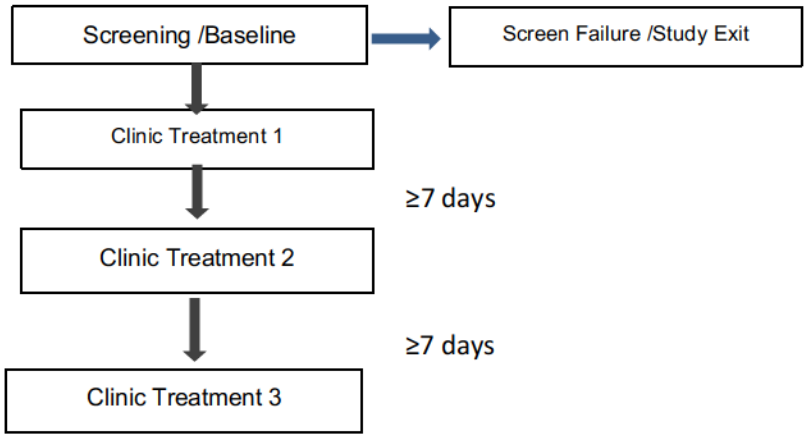
Newport Beach, CA 92660

1. DULCET STUDY PROTOCOL SYNOPSIS

Title:	Dulcet Study: A non-significant risk clinical investigation of the VibratoSleeve, a therapeutic ultrasound (TUS) phased array, for patients with ischemic and neuroischemic diabetic foot ulcers (DFU).
Design:	Prospective, single arm, open lable clinical tiral to evaluate the the feasibility of TUS in the treatment of DFU, with three different treatment levels Low, medium and high acoustic intensities, corresponding to different peak negative pressures)
Device Name and Intended Use:	VibratoSleeve is an array of single element ultrasound transducers, driven in a phased manner, and held in place externally by an adjustable sleeve. In this study, device experts will use the VibratoSleeve in a clinic setting and will evaluate for evidence of an increase in distal limb TcPO2 in adult subjects with ischemic and neuroischemic DFU.
Visit Schedule:	Visits will occur at screening (baseline data) and at three in-clinic treatment sessions, each separated by at least a 1-week interval.
Study Objectives:	The objectives of this study are: • Establish a safety profile for both the procedure and the VibratoSleeve TUS for the treatment DFU. • Gather initial evidence of the treatment and immediate post-treatment efficacy of the VibratoSleeve TUS in DFU subjects. • Request subject usability feedback: comfort, tolerability, and human factors of the VibratoSleeve assessed by questionnaire and certain human and operator factors associated with the use of the device.
Number of Subjects and Defined Point of Enrollment	Up to twelve subjects will be required for treatment and evaluation. The defined point of enrollment will be the time at which the patient signs the Informed Consent Form (ICF) to undergo screening procedures to ascertain eligibility. An estimated 50% of enrolled subjects may not satisfy all inclusion/exclusion criteria. Therefore, up to twenty-four subjects may have to be enrolled to generate twelve evaluable subjects qualified for both treatment and evaluation.
Inclusion Criteria	1. Presence of at least one DFU (grade 0 or 1 according to the University of Texas classification). 2. Diagnosis of diabetes mellitus. 3. Diagnosis of PAD that meets at least one of the following conditions: a. Ankle-brachial index (ABI) of < 0.9 in the same limb as the DFU b. Toe Brachial Index (TBI) ≤ 0.6 OR Toe Blood Pressure ≤ 50 mmHg c. Documented history of PAD for a minimum of 3 calendar months prior to time of enrollment 4. Aged ≥ 22 years
Exclusion Criteria	1. Rutherford 6 stage PAD. 2. Active DFU infection. 3. End-stage renal disease on dialysis.

	4. HbA1c > 11%. 5. Planned PAD revascularization. 6. Prior stenting in posterior tibial, anterior tibial or peroneal artery. 7. Re-vascularization procedure within 30 days prior to enrollment in the study. 8. History or diagnosis of severe chronic venous insufficiency or mixed arterio-venous disease. 9. Acute limb ischemia within 30 days prior to treatment. 10. History or diagnosis of deep venous thrombosis below the knee in treatment leg. 11. Any conditions that, in the opinion of the investigator, may render the patient unable to complete the study or lead to difficulties for patient compliance with study requirements, or could confound study data. 12. Patient's enrollment in another investigational drug or device study that has not completed the required primary endpoint follow-up period.
Safety Endpoint	To evaluate the overall safety of the VibratoSleeve TUS device for the treatment of PAD, the Principal Investigator will undertake a detailed assessment of all procedure- and/or therapy-related adverse events.
Efficacy Endpoints	• Transcutaneous Oxygen Pressure ($TcPO_2$). • Perfusion rate, as measured with the FlowMet device (Medtronic). • DFU tissue oxygenation (StO_2) and hemoglobin content (HbT2), as measured with the Clarifi device (Modulim).
Treatment	Each TUS treatment will be provided at a clinic following debridement and ulcerated wound assessment. Each subject will receive three levels of TUS treatment (low, medium, and high acoustic intensities, corresponding to different peak negative pressures). Each of the three treatments will occur on separate dates, spaced at least one week apart. The duration of each treatment level will be 90-minutes. The VibratoSleeve will be applied to the posterior calf (proximal to the TUS) using water-based acoustic coupling gel by trained clinical trial staff, and TUS delivered using Vibrato's custom generator. This study is designed to address acute changes in perfusion with each of the three TUS treatments.
Statistical Hypothesis	Statistical hypotheses will not be applied in this pilot study. Information collected during the study may be used to support a 510(k) application as well as to select the endpoints and determine sample sizes for future trials.
Study Duration	The Sponsor expects the trial to last eight months from the time the first subject enrolls until the time of the last follow-up visit.

2. STUDY FLOW CHART



3. SCHEDULE OF EVENTS

Table 1. Data collection requirements

Activity	Screening / Baseline (Day 0)	1st Treatment Session (Days 0+)	2nd Treatment Session (1st Treatment + ≥7 Days)	3rd Final Treatment Session (2nd Treatment + ≥7 Days)
Informed Consent	X			
Demographics & Medical Drug History	X			
Clinical Evaluation & Rutherford and University of Texas Classification and Calf	X			
I/E Criteria	X			
ABI/TBI	X*	X	X	X
Transcutaneous Oxygen Pressure ($TcPO_2$)		X	X	X
Perfusion of the foot: FlowMet and Clarifi devices		X	X	X
Vital Signs		X	X	X
Subject Questionnaire		X	X	X
Adverse Events	X	X	X	X
Protocol Deviations	X	X	X	X

*Only required if needed for PAD documentation (see inclusion criteria #3)

All treatment visits will be completed within 3 months of the first treatment session