# A New Heat Therapy Device for Home-based Leg Heating in Patients With Lower-extremity Peripheral Artery Disease

**NCT05335161**

**February 22, 2022**

## 1. Background and Rationale

Peripheral artery disease (PAD) is a chronic condition characterized by impaired blood flow to the lower extremities. It is prevalent in older adults and is associated with mobility impairment, pain, and increased risk of cardiovascular events. Previous studies have suggested that heat therapy may improve vascular function and limb perfusion in patients with PAD. This study aims to develop and test the feasibility of a novel home-based leg heat therapy system specifically designed for patients with lower extremity PAD.

## 2. Objectives

The primary goal of this study is to design a clinical-grade, easy-to-use leg HT system for elderly individuals suffering from PAD. Building on an existing cryotherapy water-circulating device designed for sports recovery, we will develop a new prototype system consisting of leg sleeves composed of an inner layer of polyurethane water-circulating pads and an outer layer of six inflatable bladders. The feasibility and safety of the prototype units will be evaluated in a single-arm pilot trial involving six patients with symptomatic PAD. The primary outcomes are completion rates, safety, and device usability. Secondary outcomes included changes in 6-minute walk distance, calf strength, performance on the five times sit-to-stand test, and quality of life as measured by the Walking Impairment Questionnaire (WIQ).

## 3. Participants

Patients with symptomatic PAD will be recruited through flyers, online advertisements, and referrals from local peripheral vascular disease clinics. Men and women 60 years or older with a resting ABI of $\leq$0.90 in at least one leg were included in the study. Individuals with a resting ABI of >0.91 at baseline will be eligible if their ABI decreases by $\geq$20% after a heel-rise test. The exclusion criteria include the presence of critical limb ischemia (ischemic rest pain or ischemia-related, nonhealing wounds, or tissue loss), prior leg amputation, exercise tolerance limited by factors other than leg pain (eg, angina, arthritis, severe lung disease, etc), recent lower extremity revascularization or orthopedic surgery, use of a walking aid other than a cane, active cancer, chronic kidney disease (estimated glomerular filtration rate of <30), inability to fit into water-circulating trousers, a Mini-Mental Status Examination score of <23, and impaired thermal sensation in the leg.

## 4. Experimental protocol

Participants will attend two baseline laboratory visits. Before each session, they will be instructed to fast overnight, avoid exercise for 24 hours, and refrain from smoking for 4 hours. During the first visit, participants will receive informed consent, complete a medical history form, have their leg symptoms assessed using the San Diego Claudication Questionnaire, complete the Mini-Mental Status Examination, and undergo a thermal sensation test with heating pads on their thighs and calves. The ABI will be assessed following American Heart Association guidelines. After a 10-minute rest, a handheld Doppler ultrasound probe will be used to measure systolic pressures in the posterior tibial, dorsalis pedis, and brachial arteries. The ABI for each leg will be calculated

by dividing the average dorsalis pedis and posterior tibial pressures by the average brachial pressures. Participants will then be familiarized with the 6-minute walk test, isokinetic calf strength testing, and the five-times sit-to-stand test.

The second visit, conducted at least 48 hours later, will include (1) blood pressure measurement, (2) a 6-minute walk test, (3) torque assessments of the plantar flexors using an isokinetic dynamometer, (4) the five-times sit-to-stand test, and (5) quality of life assessment via the WIQ. After completing baseline tests, participants will undergo a supervised 90-minute treatment session with the prototype HT device to monitor acute changes in skin temperature and blood pressure. Thermocouples (MLT422; AD Instruments, Colorado Springs, CO) will be taped to the calf and thigh to measure leg skin temperature, and systolic and diastolic blood pressures will be recorded every 5 minutes.

Participants will be given the prototype device for daily use while lying down or seated with legs extended. They will log therapy sessions and measure blood pressure before and after each session using a portable monitor (Omron 3 Series Upper arm, Omron Healthcare Co. Ltd., Kyoto, Japan). Weekly check-ins with the study coordinator will track therapy dates, times, blood pressure readings, and any adverse effects. Outcomes will be reassessed at the end of the 12-week intervention, with participants stopping treatment 48 hours before the final evaluations to isolate chronic effects.

## 5. Outcome measures

Feasibility end points (primary outcomes)

The completion rate will be determined by monitoring the number of participants who finish the study protocol within the specified timeframe compared to the total number enrolled in the study.

Safety: Safety will be evaluated by monitoring adverse events. The research coordinator will call patients weekly to record any adverse events during the intervention.

Device usability: Participants will be asked to rate the device usability at the end of the experiment using the System Usability Scale. The psychometric properties of the System Usability Scale have been established, including its reliability and sensitivity.

Secondary outcomes

6-Minute walk test: Participants will receive standardized instructions and be asked to walk the greatest distance possible by walking back and forth along a 100-ft corridor for 6 minutes.

Blood pressure: Blood pressure measurement will be conducted using an automated device (Tango+, Suntech Medical, Morrisville, NC), following the recommendations of the American Heart Association.

Calf strength: Torque assessments of the plantar flexors of the most symptomatic leg or the leg with the lowest ABI will be conducted using an isokinetic dynamometer (Biodex System 4 Pro, Biodex Medical Systems, Shirley, NY). The participants will be positioned supine on the

dynamometer chair with their knees flexed at 90°. Before maximal testing, they will complete a standardized warm-up consisting of three submaximal contractions, each held for 5 seconds at approximately 50% of perceived maximal effort. Following the warm-up, participants will perform three maximal voluntary isometric contractions, each lasting 5 seconds, with a 60-second rest period between attempts to minimize fatigue. Standardized verbal encouragement will be provided during each maximal voluntary isometric contraction to ensure maximal effort. The trial that produces the highest peak torque value (in N·m) will be selected for analysis.

The Five Times Sit-to-Stand Test: Participants are asked to sit in a chair with arms folded across their chest and stand five times in a row as quickly as they can. The time it takes to complete five chair rises is recorded.

WIQ: Patient-reported perceptions of walking ability will be assessed using the WIQ. This disease-specific questionnaire assesses the ability of patients with PAD to walk defined distances and speeds and to climb stairs, with scores ranging from 0 to 100.30 Higher scores reflect better community-based walking ability.

**6. Statistical analysis**

This small pilot trial aims to test prototype HT devices and evaluate their safety and feasibility in patients with PAD. The main goal is to gather initial data to refine device design and guide the development of future large-scale studies. Due to the exploratory nature of this trial, no power analysis was performed. Changes in each outcome from baseline to the 12-week follow-up will be compared using paired two-sample t-tests. A two-sided P value of $<.05$ will be regarded as statistically significant. Before starting the intervention, participants will undergo a supervised HT session, during which skin temperature and blood pressure will be monitored every 5 minutes throughout the 90-minute session. Skin temperature and blood pressure responses during this session will be analyzed using repeated-measures analysis of variance. When a significant main effect is found, Sidak multiple comparisons tests will evaluate differences between time points relative to baseline. A P value of $<.0028$ will be considered statistically significant for the Sidak-adjusted comparisons. All statistical analyses will be conducted using Prism 10 (Version 10.3.0 (461)).