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A Momentum-Enabled Treadling Methodology to Improve Gait and Enhance Mobility in Patients with Peripheral Arterial Disease

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1. ABSTRACT

A significant cause of mobility impairment in the elderly is peripheral arterial disease (PAD). PAD results in significant functional decline, reduced walking speed and distance, and lower physical activity levels, resulting in a loss of independence and impaired quality of life. The most effective therapy for PAD is rigorous exercise (e.g., walking). However, most PAD patients will not participate in supervised exercise, and walking-related pain provides a substantial barrier to unsupervised exercise, resulting in a lack of compliance. In addition, common comorbidities act as difficult-to-surmount barriers to rigorous physical exercise.

Treadwell Corporation is pioneering an innovative treadling methodology and device (the TREDLR) to provide a therapy that can improve exercise tolerance in patients with PAD, accelerating their progress to reaping the functional benefits of more rigorous physical exercise. The TREDLR contains an internal flywheel that generates momentum while the user initiates repetitive ankle flexion and extension movements.

Preliminary studies with the TREDLR prototype have demonstrated clear hemodynamic improvements in the lower extremities of participants who treadle. Additional pilot data from the collaborating sub-award PI, Dr. Jason Franz, have demonstrated in part that treadling affords the same ankle and calf muscle fascicle kinematics as walking without comparable levels of muscle activation – a finding that we posit will translate to improved compliance and prolonged participation prior to onset of discomfort in people with PAD. We hypothesize that this will improve patients' functional exercise capacity and accelerate their progress to participation in more rigorous exercise therapy.

In this Phase I STTR, the investigative team evaluated this novel treadling methodology in individuals aged over 65 years with and without diagnosed PAD. To accomplish several early and critical milestones, this study evaluated joint and muscle kinematic differences between treadling and conventional exercise (**Aim 1**), explored improvements in mobility and functional exercise capacity in individuals who treadle as compared to a control cohort (**Aim 2**), and assessed user affect that may impact compliance and, ultimately, widespread adoption (**Aim 3**).

Summary of results. This Phase I study yielded strong support for the hypothesis outlined for Aim 1 and modest support for the hypotheses outlined for Aim 3. The feasibility of Treadwell's proprietary treadling methodology as a method to improve exercise tolerance and mobility in older adults with and without PAD has not been objectively established in this Phase I study. However, promising results from other aims and large inter-individual variation supports continued study with designs that would encourage personalized prescription to those that would most benefit from device use. We also consider the results outlined in this report an early proof of concept that in-home use of the TREDLR prototype is feasible for widespread adoption.

2. BACKGROUND AND SIGNIFICANCE

A significant cause of mobility impairment in the elderly is peripheral arterial disease (PAD)[1], a chronic arterial occlusive disease that affects 20 – 30%[2] of adults aged over 65 years. Intermittent claudication, a frequent PAD symptom, results in significant functional decline, reduced walking speed and distance, and lower physical activity levels[3-10], resulting in a loss of independence and impaired quality of life[11].

The most effective therapy for PAD is rigorous exercise (e.g., walking). However, most PAD patients will not participate in supervised exercise[12], and walking-related pain provides a substantial barrier to unsupervised exercise, resulting in a lack of compliance. In addition, common comorbidities (e.g. diabetes) act as difficult-to surmount barriers to physical exercise[13].
Treadwell Corporation is pioneering an innovative treadling methodology and device (the TREDLR) to provide a therapy that can improve exercise tolerance in patients with PAD, accelerating their progress to reaping the functional benefits of more rigorous physical exercise.

The TREDLR contains an internal flywheel that generates momentum while the user initiates repetitive ankle flexion and extension movement. This movement activates the calf muscle pump and improves blood flow in the lower extremities[14-15]. The improved blood flow as the potential to address the hemodynamic insufficiency in PAD, as under-perfused muscular segments result in pain during physical activity, which disproportionately afflicts the calf muscles[16-17].

Treadwell's technology affords several differentiating breakthroughs. 1) Treadling does not result in oxygen deprivation in the muscles (non-fatiguing) and is therefore unlikely to cause pain. 2) Improved hemodynamics can increase blood perfusion in the limbs, which research has suggested may improve oxidative capacity of the skeletal muscles[18]. 3) The user-recruited motion can increase compliance. For these reasons, we hypothesize that repetitive, non-fatiguing engagement of the calf muscle tendons involved in treadling will improve patients' functional exercise capacity and allow them to progress to participation in rigorous exercise therapy.

Preliminary studies with the TREDLR prototype have demonstrated patient-reported improvements in gait, balance, and mobility in geriatric patients. Additional pilot data have demonstrated in part that treadling affords the same ankle and calf muscle fascicle kinematics as walking without comparable levels of muscle activation – a finding that we posit will translate to improved compliance and prolonged participation prior to onset of discomfort in people with PAD. In this Phase I STTR, the investigative team will evaluate this novel treadling methodology in individuals aged over 65 years with previously diagnosed PAD. To accomplish several early and critical milestones, this study will evaluate joint and muscle kinematic differences between treadling and conventional exercise (Aim 1), explore improvements in mobility and functional exercise capacity in individuals who treadle as compared to a control cohort (Aim 2), and assess user attitude toward device use that may impact compliance (Aim 3).

3. SPECIFIC AIMS

Specific Aim 1: Quantify joint and muscle differences between treadling and conventional exercise. To gather important benchmark mechanistic knowledge, we will collect the following measurements while subjects walk, cycle or treadle: i) ankle joint kinematics; ii) calf muscle fascicle behavior; iii) number of muscle stretch-relaxation cycles; and iv) muscle activity. *Success Metric:* Ankle joint muscle kinematics are comparable for walking, cycling, and treadling, but muscle activity during treadling (measured by EMG) will be lower than for walking/cycling.

Specific Aim 2: Investigate improvements in mobility in PAD subjects who treadle. At baseline, we will quantitatively assess overground walking speed, 6-min walk distance, time-to-onset of discomfort, and underlying gait mechanics (e.g., stride length, peak ankle power[19]). Individuals will then be randomized to a treadling group or a control group who are instructed to continue their normal exercise. Treadling subjects will treadle 3x per week (15-minute sessions) for 6 weeks. Provided pedometers will be used to follow daily activity. Baseline metrics will be repeated at the conclusion of the trial, and pre/post comparisons will evaluate improvement vs. controls. *Success Metric:* Minimal detectable improvements in 6-minute walk test and overground walking speed for the treadling group.

Specific Aim 3: Evaluate subject attitude toward treadling. The treadling group will answer a 5-point Likert style questionnaire at the conclusion of the trial. Surveys will address perceived ease of use and attitude toward continuing the intervention to provide insight to future compliance. *Success Metric:* >80% of users will report 3 or higher for "would continue to use" and >70% will report 3 or higher for "would recommend to others".

Impact: This Phase I project successfully demonstrated the feasibility of incorporating Treadwell's proprietary treadling methodology in an intervention designed to improve exercise tolerance and mobility in older adults with and without PAD, including baseline comparisons to other routinely prescribed interventions. These results provide preliminary evidence to support more rigorous clinical trial testing coupled with mechanistic outcomes in Phase II.

4. EXPERIMENTAL APPROACH

4.1. Participants. Our original participant recruitment goal was 30 subjects, of which 15 would be randomly assigned to a control group and 15 would be randomly assigned to a treadling group for Aims 2 and 3. However, the COVID-19 pandemic halted our recruitment of new subjects in March 2020. At that time, we had successfully enrolled a total of 17 older adult subjects to participate in this research study and randomly assigned those based on enrollment to the control or treadling groups after providing written, informed consent according to the University of North Carolina Biomedical Sciences IRB. **Table 1** summarizes those recruitment demographics. All of these subjects participated in the procedures summarized in Aim 1. However, at the time of study stoppage, 5 subjects were participating in the 6-week randomized controlled trial and did not complete the study. Thus, a total of 13 subjects (5 controls and 8 treadling subjects) completed the procedures summarized in Aims 2 and 3. **Table 2** summarizes those recruitment demographics. This final cohort of subjects included four older adults with peripheral arterial disease (age: 65+ years; 3M/1F) and nine older adults without peripheral arterial disease (age: 65+ years; 5M/4F). Subjects met the inclusion criteria of the study if they were age 65 years or older, able to walk without an assistive device, had the capacity to provide written informed consent, and had previously been diagnosed with peripheral arterial disease (PAD cohort only). Subjects were excluded from the study if they sustained a leg injury or fracture within the last 6 months, had a leg prosthesis, were a prisoner, lacked the ability to give informed consent, or had a self-reported vestibular impairment.

Table 1. Recruitment Demographics (total sample)

	Control Group (n=7)	Treadling Group (n=10)
Age (Years)	71.3 ± 5.2	72.3 ± 5.5
Gender Demographics	Male - 3	Male - 6
	Female - 4	Female - 4
Race Demographics	White/Caucasian - 7	White/Caucasian - 8
	Black or African American - 0	Black or African American - 1
	American Indian or Alaskan Native - 0	American Indian or Alaskan Native - 1
	Other - 0	Other - 0
Ethnicity Demographics	Non-Hispanic or Latino -7	Non-Hispanic or Latino - 10
	Hispanic or Latino - 0	Hispanic or Latino - 0

Table 2. Recruitment Demographics (Aims 2 and 3)

	Control Group (n=5)	Treadling Group (n=8)
Age	71.6 ± 5.0	71.6 ± 5.4
Gender Demographics	Male - 2	Male - 5
	Female - 3	Female - 3
Racial Demographics	White/Caucasian - 5	White/Caucasian - 7
	Black or African American - 0	Black or African American - 1
	American Indian or Alaskan Native - 0	American Indian or Alaskan Native - 0
	Other - 0	Other - 0
Ethnicity Demographics	Non-Hispanic or Latino -5	Non-Hispanic or Latino - 8
	Hispanic or Latino - 0	Hispanic or Latino - 0

4.2 Summary of Experimental Design. We recruited subjects via flyer, email, and word of mouth. Any subject that showed interest in participating were invited to take part in a phone screening that determined basic study eligibility (*See Appendix 1*). Eligible participants were then invited to participate in the remainder of the study while ineligible participants were informed of their results and their answers to the telephone screening were immediately destroyed. Eligible participants were then placed into study groups based on their diagnosis of PAD. Each participant filled out a study consent form (*See Appendix 2*) and received a Fitbit to monitor activity levels during waking hours beginning at least one week prior to their initial laboratory visit.

At the initial visit, subjects walked through timing gates to determine their preferred overground walking speed (PWS). Subjects then completed a randomly ordered series of exercises, including walking at PWS, biking, and treadling. After the exercises were complete, subjects then took part in a 6-minute walk test – a common clinical method to quantify mobility levels in patients with PAD. Subjects were then randomly assorted trial groups that determined the activities they would perform over the next 6 weeks. "Control" participants were asked to live out their normal daily lives for 6 weeks while "Treadling" participants were asked to use the TREADLR® 3 times a week for 15-minute sessions under the supervision of a study team member. Upon conclusion of the 6 weeks, subjects returned to the laboratory and performed the same exercises from the previous visit in a randomly determined order. Afterwards, they completed a 6-minute walk test.

After the second laboratory visit, subjects wore their Fitbit for another week to determine post-intervention physical activity levels. Once the week is over, subjects returned their Fitbit and received compensation for their time. Treadling participants were also asked to complete a post-participation survey that asked questions regarding the effectiveness of the TREADLR® device (*See Appendix 3*). A summary of the study process as a whole is depicted below in **Figure 1**.

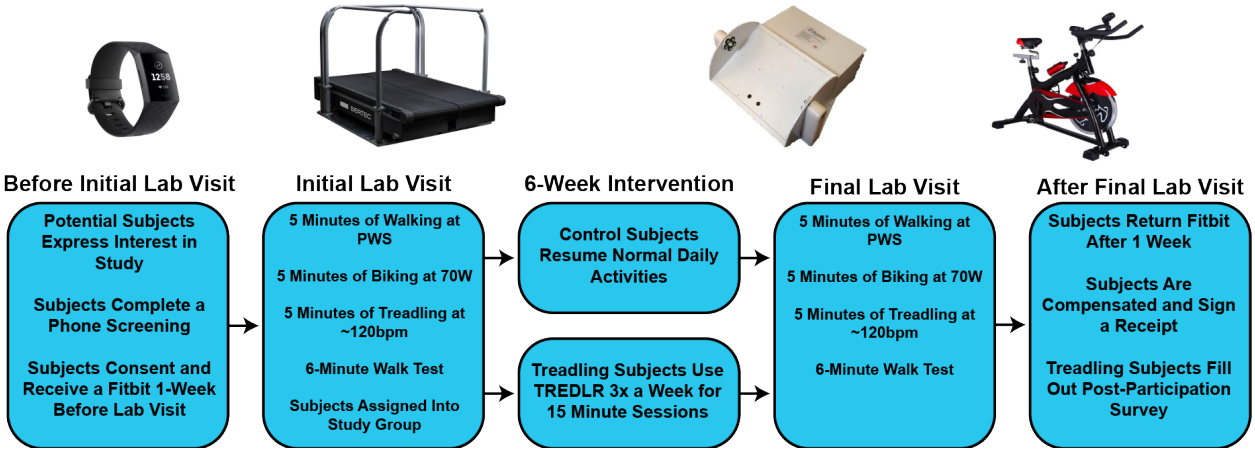

Figure 1. Summary of experimental design and overall workflow.

4.3 Measurement and Analysis. Using a photo cell timing system along an instrumented straight walkway, we determined each subjects' preferred overground walking speed (i.e., PWS) as the average of 3 times taken to walk 30 m. Subjects then completed three 5-minute experimental trials in fully randomized order: walking at their PWS, biking at approximately 70 W, and treadling at a comfortable rate of, on average, 122±21 (i.e., Mean ± SD) cycles per second. The following

measures were collected during each of these experimental trials using techniques described in more detail below: the motion of subjects' torso, pelvis, and legs (measure using 3D motion capture), leg muscle activity patterns (measured using electromyography), and fascicle lengths and velocities of the medial gastrocnemius and soleus muscles (measured using *in vivo* cine B-mode ultrasound). Due to the nature of ultrasound image analysis, those data not included in this report and will follow once complete. We collected EMG data from the following muscles: lateral gastrocnemius, soleus, and tibialis anterior. Prior to EMG sensor placement, subjects' skin was cleaned with alcohol, and shaved when necessary to improve sensor recording ability. During the walking trial, forces between the subjects' feet and ground were collected via a dual-belt force-measuring treadmill (Bertec, Columbus, OH). We also identified individual steps using a 20N vertical GRF threshold as a reference for heel-strike. For subjects with PAD, we assessed the onset of claudication discomfort during each trial using the Claudication Symptom Rating Scale. These participants verbalized a number from 1 to 5 (1 indicating no pain and 5 indicating unbearable pain) at each minute mark. Lastly, subjects completed a 6-minute walk test along a 30-m hallway. We instructed subjects to walk as far as they could safely walk in the time allotted, a test used to objectively assess walking capacity. For participants with PAD, they were asked to signal the respective numbers from the Claudication Symptom Rating Scale as the onset of claudication discomfort progressed throughout the trial. Study team members also recorded the time it took until subjects verbalized a new number on the Claudication Symptom Rating Scale.

During all laboratory exercises (excluding the 6-minute walk test), a 16-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA) operating at 100 Hz recorded pelvis and lower extremity kinematics via 17 anatomical markers and an additional 14 tracking markers affixed using rigid clusters. A standing trial, as well two unilateral hip circumduction trials used to estimate functional hip joint centers (Piazza et al., 2001), also included markers placed on the left and right medial knee and malleoli. Marker trajectories and ground reaction forces (GRF) (walking trial only) were filtered using 4th order low-pass Butterworth filters with cutoff frequencies of 6 Hz and 20 Hz, respectively. EMG signals, collected from the medial gastrocnemius, soleus, and tibialis anterior, were bandpass filtered using cutoff frequencies of 20 Hz (high pass) and 400 Hz (low pass). We then used the static standing calibration and functional hip joint centers to scale a seven segment, 18 degree-of-freedom model of the pelvis and right and left legs (Arnold et al., 2010). We used this model and the filtered marker and force data to estimate joint angles, moments, and powers of the lower limb joints using an inverse dynamics routine described in detail previously (Browne and Franz, 2019). We extracted marker trajectories, EMG signals, and GRFs from the bilateral, cycle-averaged profiles.

4.4 Statistical Analysis. For all data sets, we used Shapiro-Wilks tests confirmed normal distributions. In our Aim 1 analysis, we used a repeated measures ANOVA to evaluate between-condition effects on peak dorsiflexion and plantarflexion angles, ankle range of motion, and plantarflexor and tibialis anterior muscle activity. For Aim 2, a mixed factorial ANOVA tested for significant main effects of group (treadling vs. control) and time (pre vs. post) on each subject's 6-minute walk test distance and calculated PWS. Exploratory paired-samples t-tests explored pre-post effects within each cohort of subjects. In addition, for subjects with PAD, we qualitatively compared the time until onset of claudication during each 6-minute walk test. Lastly, we calculated percentages to determine the number of subjects reporting anticipated scores or higher on each survey response to achieve Aim 3 milestones.

5. SUMMARY OF STUDY RESULTS

This section reports our study results for primary and secondary outcome measures organized by specific aim. For our analysis, we opted to combine all PAD and non-PAD participants into one cohort due to recruitment restrictions following the COVID-19 pandemic. However, we provide individual subject data for follow-on analyses as needed.

5.1. Aim 1: Quantify joint- and muscle-level differences between treadling and conventional exercise. Compared to conventional exercises such as walking and cycling, there were no significant differences in peak ankle dorsiflexion ($p \geq 0.150$) for treadling exercise. Alternatively, peak ankle plantarflexion was 18.5° larger for treadling than for walking and cycling ($p \leq 0.018$). Total ankle range of motion during treadling did not differ significantly from that during cycling (Cycling: 12.5°, Treadling: 14.5°, $p=0.622$), but was 57% smaller than that during walking (28.7°, $p=0.002$) for all subjects. **Figure 2** summarizes subject-average ankle angle profiles during each exercise modality.

Peak soleus and lateral gastrocnemius muscle activity did not significantly differ between treadling and cycling ($p \geq 0.511$). However, treadling subjects exhibited 73% smaller peak soleus muscle activity and 79% smaller peak lateral gastrocnemius activity than walking (p-values<0.001). Treadling subjects exhibited 65% smaller peak tibialis anterior activity compared to walking

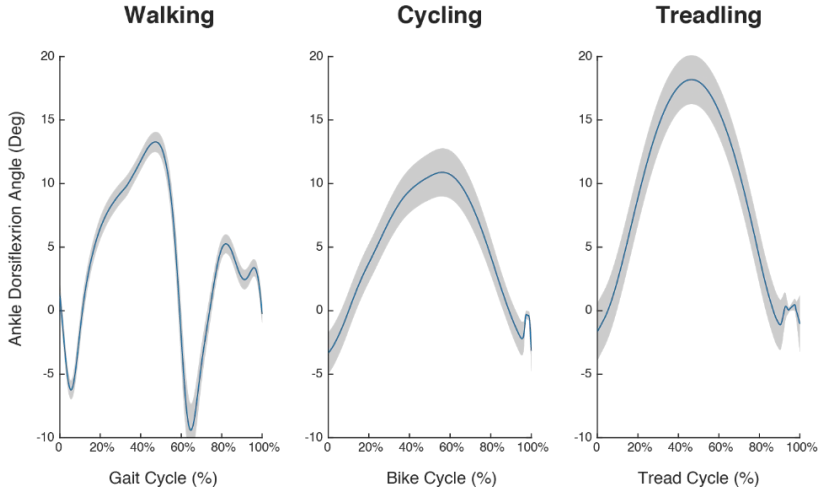

Figure 2. Subject-average ankle angle kinematic profiles. Shading shows ± standard error of the subject average.

($p<0.001$), but 66% more peak tibialis anterior activity compared to cycling ($p=0.002$). **Figure 3** summarized these electromyographic comparisons.

Aim 1 conclusions: Data from this Phase I study provides strong support for the hypothesis that ankle joint kinematics are comparable between walking, cycling, and treadling, but that muscle activity during treadling was substantially lower than for walking/cycling. Following their analysis, which is incredibly time intensive, we anticipated muscle-level outcomes derived via ultrasound to provide additional mechanistic support for this hypothesis. Together, these data will support the efficacy of treadling to effectively target calf muscle and ankle joint mechanics with little activation, thereby serving as an important step in the return to more rigorous exercise.

5.2. Aim 2: Investigate improvements in mobility in PAD subjects who treadle. Using the TREADLR® for 6 weeks did not have a statistically significant effect on 6-minute walk distance nor on preferred walking speed (p-values≥0.348), and their response did not differ significantly from control subjects. Although we consider it unlikely based on our interpretation of the available data, we cannot exclude the possibility that these statistical outcomes are influenced by the smaller than anticipated sample size. Thus, to more carefully report the study data, and in the spirit of transparency, we follow here by reporting and assessing individual subject outcomes. **Table 3** summarizes these for our primary outcomes. Overall, a small majority of participants (8/13; 62%) improved their 6-minute walk distance following at post-test compared to baseline, while 54% (7/13) increased their PWS. Of the participants that participated in the treadling intervention, 5/8 (63%) improved their 6-minute walk distance compared to baseline. However, only 3/8 (38%) treadling participants improved their PWS following the intervention compared to baseline. For participants in the control group who continued their normal physical activity, 3/5 (60%) improved their 6-minute walk distance while 4/5 (80%) improved their PWS. Nevertheless, we noted considerable interindividual variance in these outcomes that could inform the design of future studies.

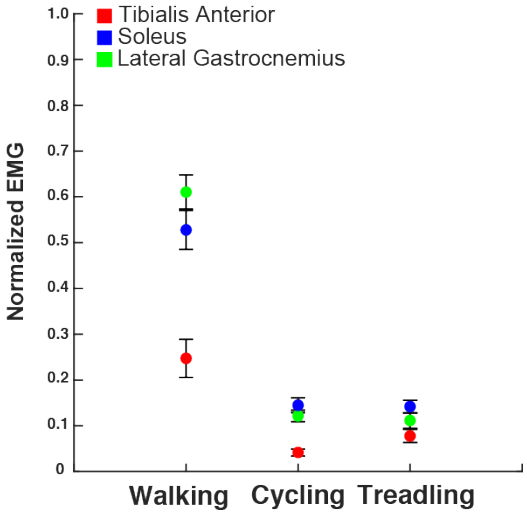

Figure 3. Group average (SE) peak lower leg muscle activities for each exercise modality studied in Specific Aim 1.

Table 3. Individual subject data summarizing the results of 6-weeks of trealing versus controls on primary outcomes.

ID	Group	Baseline		Post-Test		Δ 6-min walk Distance (m)	Δ PWS (m/s)
		6-min Walk Distance (m)	PWS (m/s)	6-min Walk Distance (m)	PWS (m/s)		
Non-PAD04	Control	473.0	1.01	480.0	1.09	7.0	0.08
Non-PAD05	Control	638.0	1.38	614.6	1.52	-23.4	0.14
Non-PAD07	Control	557.5	1.39	630.0	1.45	72.5	0.06
Non-PAD09	Control	656.5	1.30	691.3	1.35	34.8	0.05
Non-PAD01	Tread	647.9	1.56	677.0	1.32	29.2	-0.24
Non-PAD02	Tread	573.9	1.29	609.8	1.14	35.9	-0.15
Non-PAD03	Tread	546.1	1.24	522.3	1.27	-23.8	0.03
Non-PAD06	Tread	471.3	1.37	570.0	1.34	98.7	-0.03
Non-PAD08	Tread	600.0	1.52	605.1	1.56	5.1	0.04
PAD04	Control	502.9	1.32	492.2	1.10	-10.7	-0.22
PAD01	Tread	557.5	1.39	615.5	1.41	58.0	0.02
PAD02	Tread	520.3	1.27	456.1	1.27	-64.2	0
PAD03	Tread	420.0	0.83	389.9	0.79	-30.1	-0.04
Total	**Control**	**565.6 ± 80.7**	**1.28 ± 0.16**	**581.6 ± 91.9**	**1.30 ± 0.20**	**16.0 ± 38.4**	**0.02 ± 0.14**
	Tread	**542.1 ± 71.2**	**1.31 ± 0.22**	**555.7 ± 94.4**	**1.26 ± 0.23**	**13.6 ± 52.6**	**-0.05 ± 0.10**

For our key secondary outcomes, we noted no significant session (pre vs. post) or group×session interaction on stride length nor peak ankle power output during the push-off phase of walking. These outcomes are summarized in Table 4.

Table 4. Secondary Biomechanics Outcomes (Specific Aim 2)

	Control Subjects		Treadling Subjects	
Outcome Measure	**Baseline**	**Post-Test**	**Baseline**	**Post-Test**
Stride Length (m)	1.27 ± 0.14	1.27 ± 0.15	1.38 ± 0.15	1.38 ± 0.15
Peak Ankle Power (W/kg)	2.60 ± 0.83	2.63 ± 1.00	2.64 ± 0.75	2.43 ± 0.92

Aim 2 conclusions: The feasibility of Treadwell's proprietary treadling methodology as a method to improve exercise tolerance and mobility in older adults with and without PAD has not been objectively established in this Phase I study. However, together with promising outcomes from Aim 1 and the relatively large inter-individual variation, continued study toward personalized prescription to those that would most benefit from device use may be warranted.

5.3. Aim 3: Evaluate subject attitude toward treadling.

The following summarizes the results of our objective questionnaire administered to all participants in the treadling intervention. We note here that the scales ranged from 1 (strongly disagree) to 5 (strongly agree). Of the subjects that used the TREADLR® for 6 weeks, all reported a 4 or higher on the question asking if the device was "easy to use". Moreover, all subjects reported a score of 5 on the statement, "The device was comfortable during use". All subjects also indicated a 3 or higher stating that the device was "non-fatiguing". 5/7 (71%) of all treadling participants indicated a 3 or higher on "treadling was effective at decreasing daily discomfort". However, only 2/7 (29%) participants indicated that treadling was effective at enhancing mobility. The same number of subjects 2/7 (29%) indicated a 3 or higher when asked if they would "continue to use the device". All subjects indicated a 3 or lower when prompted if there was any "discomfort" or "negative events" as a result of the intervention. Finally, a very promising (6/7) 86% participants reported a 3 or higher when asked if they would "recommend the device to others". A complete breakdown of survey results are summarized below and organized by question and subgroup.

The device was easy to use:
3/3 (100%) PAD participants reported 5
4/4 (100%) non-PAD participants reported 4 or higher

The device was comfortable on the ankle during use:
3/3 (100%) PAD participants reported 5
4/4 (100%) non-PAD participants reported 5

The device was non-fatiguing:
3/3 (100%) PAD participants reported 3 or higher
4/4 (100%) non-PAD participants reported 4 or higher

Treadling was effective at decreasing daily discomfort:
3/3 (100%) PAD participants reported 3 or higher
4/4 (100%) non-PAD participants reported 3

Treadling was effective at enhancing mobility:
2/3 (66%) PAD participants reported 3 or higher
3/4 (75%) non-PAD participants reported 3 or higher

I would opt to treadle if given the opportunity:
2/3 (66%) PAD participants reported 3 or higher
3/4 (75%) non-PAD participants reported 3 or higher

There was discomfort or other negative events as a result of the intervention
2/3 (66%) PAD participants reported 3 or higher
0/4 (0%) non-PAD participants reported 3 or higher

I would recommend this device to others:
3/3 (100%) PAD participants reported 3 or higher
3/4 (75%) non-PAD participants reported 3 or higher

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APPENDIX 1. Human Subjects Informed Consent Form

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: __7/02/2019_____
IRB Study # 18-3169
Title of Study: A momentum-enabled treadling methodology to improve gait and enhance mobility in patients with peripheral arterial disease
Principal Investigator: Jason Franz
Principal Investigator Department: Biomedical Engineering - Undergraduate
Principal Investigator Phone number: (919) 966-6119
Principal Investigator Email Address: jrfranz@email.unc.edu
Funding Source and/or Sponsor: Treadwell Corporation

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Rigorous exercise is the gold standard to improve mobility, pain-free walking time, and independence in people with peripheral arterial disease. Accelerating progress to and improving compliance with rigorous exercise treatment has the potential to substantially improve patient mobility and independence. The purpose of this study is to test whether a simple new exercise device that promotes ankle rotation can improve exercise tolerance and walking ability in people with peripheral arterial disease.

You are being asked to be in the study because you are an adult older than 65 years, you may have previously diagnosed peripheral arterial disease, and you can walk without an assistive device (e.g., cane or walker).

Are there any reasons you should not be in this study?
You should not be in this study if you have had a leg injury or fracture in the last 6 months, or have a leg prosthesis (i.e., artificial leg or leg joint).

How many people will take part in this study?
There will be approximately 60 people in this research study.

How long will your part in this study last?
If you agree to participate in this study, you would visit our lab twice. The lab visits will take place at the UNC Applied Biomechanics Research Laboratory located in 10306 Mary Ellen Jones Building. Initial baseline and follow up visits may last up to 3 hours each. Some participants will be invited to participate in 15 min of mild ankle exercises 3 times per week for 6 weeks in their own community.

What will happen if you take part in the study?
If you agree to participate in this study, you would complete several walking tasks, bicycling tasks, and seated ankle exercises. We will measure the electrical activity of your muscles using recording electrodes placed on your skin. Prior to the sensor placement, your skin will be cleaned with alcohol and may be shaved to improve the sensors recording abilities. We will measure the forces that you exert on the ground and will attach small reflective balls to your skin so that we can record your leg and body movements using special cameras. We will also use an ultrasound probe placed on the surface of your skin to track the motion of your calf muscles while you walk, bike, or perform the ankle exercises. Some participants will be invited to participate in 15 min of mild ankle exercises 3 times per week for 6 weeks. This will happen at your retirement community.

We will also collect the following information about you for this research study:

1. Birthdate, phone number, email, gender, height, and body weight.
2. General physical health statement, which will ask you about: weekly exercise, neurological conditions, medication use, any prosthesis (e.g., artificial leg or leg joint), and broken leg bones.

What are the possible benefits from being in this study?
You will receive some physical exercise by participating. Subjects invited to participate the ankle exercise program may benefit from increased engagement of their calf muscles, which is important for anyone seeking to preserve or enhance walking performance. Research is designed to benefit society by gaining new knowledge. Society may benefit from the findings of this study as they may lead to opportunities for approaches to enhance or preserve mobility and independence.

What are the possible risks or discomforts involved from being in this study?
The potential risks to you include the following:

a. There is some risk of stumbling or falling while walking on the treadmill. To minimize this risk, you will be instructed in proper safety procedures before the treadmill is turned on, which include always using the handrails when the treadmill is starting or stopping.

b. You may experience some mild skin irritation from the placing or removing the recording electrodes.

c. There is a risk of breach of confidentiality concerning your data. This risk is minimized by coding the data we collect and storing it separate from identifiers associated with you.

All ultrasound machines in use at the University of North Carolina have acoustic output levels that fall within the FDA guidelines. All systems, features, and accessories that will be used in the scanning of subjects under this protocol will be operating within the limits set in these guidelines. Researchers and regulatory officials have also concluded that diagnostic ultrasound poses minimal risk to patients, fetuses, and operators; and no confirmed biological effects have been reported at output levels typical of those used in human examinations.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
The information collected from you during this study will be used by the researchers and research staff of the University of North Carolina at Chapel Hill. Study team members at Carol Woods Retirement Community will also have access to this information.

Every effort will be made to protect this information from disclosure. At the initial session you will be assigned a unique participant number that will be used throughout the study. Your personal identity will not be revealed in publications that may result from this study, nor will your name be used in other research communications such as lectures at scientific meetings. Experimental data as well as personal data on the Health Questionnaire will be kept by the investigators in a secure location and will not be released in any way that could be identified with you personally.

This consent form which contains your personal information, will be stored in a secured location accessible only to the Principal Investigator or approved designee.

Participants will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?

You will be receiving $12 per hour for taking part in this study. For those participants invite to participate in the exercise intervention, you will receive an additional $50 if you complete that part of the study. You will be paid after you complete the study. Should you withdraw, or be withdrawn by the investigators, you will be paid a prorated hourly rate up to your time of withdrawal.

Will it cost you anything to be in this study?
If you enroll in this study, you will have costs which include your own travel costs (i.e., gas, bus fare). You will also receive a voucher for parking on the UNC Chapel Hill campus to cover your visits to our laboratory.

Who is sponsoring this study?
This research is funded by Treadwell Corporation via a grant from the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.
Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____
Signature of Research Participant Date

_____
Printed Name of Research Participant

_____ _____
Signature of Research Team Member Obtaining Consent Date

_____
Printed Name of Research Team Member Obtaining Consent

APPENDIX 2 – Health Questionnaire

Health Questionnaire

A momentum-enabled treadling methodology to improve gait and enhance mobility in patients with peripheral arterial disease.

Personal Information

Today's Date_____ Subject ID_____

Age_____ Sex □ Male
□ Female

Body Weight:_____

Symptoms or Signs Suggestive of Disease

Check the appropriate box:

Yes	No		
□	□	1.	Have you experienced unusual chest pain or shortness of breath at rest, during usual activities, or during mild-to-moderate exercise (e.g., climbing stairs, carrying groceries, brisk walking, cycling)?
□	□	2.	Do you have any problem with balance or dizziness?
□	□	3.	Have you experienced an unusual and rapid throbbing or fluttering of the heart?

Medical History

4. Please check which of the following conditions you have had or now have. Check as many as apply.

	Medical Condition		**Medical Condition**
□	Stroke or mini-stroke	□	Polio
□	Signs of cardiovascular disease	□	Myasthenia gravis
□	Cardiac arrhythmia	□	Pain while walking
□	Peripheral neuropathy in legs and feet (such as numbness, tingling, or burning)	□	Use of a pacemaker
□	Severe arthritis in legs which impairs normal function (such as walking)	□	Use of a prosthetic
□	Parkinson's disease		
□	Spine disk disease, ridiculopathy, or spine surgery		
□	<u>Peripheral Arterial Disease (PAD)</u> If you have PAD – when were you diagnosed _____		

5.Please list and describe what types of PAD symptoms you notice and their frequency:

_____
_____
_____

6. Please list and explain any other neurological or vestibular conditions:

_____
_____
_____

7. Please list and explain any other orthopedic disorders (including bone fractures or ligament/tendon injury within the last six months, any joint replacement surgery, or severe arthritis):

_____
_____
_____

Physical Fitness/Physical Activity

8. Considering a typical **7-day period** (1 week), how many times on average do you perform the following types of exercise for **more than 15 minutes**?

	Times Per Week
Strenuous Exercise (Heart Beats Rapidly) (e.g. running, jogging, cross country skiing, vigorous bicycling)	_____
Moderate Exercise (Not Exhausting) (e.g. fast walking, easy bicycling)	_____
Mild Exercise (Minimal Effort) (e.g. yoga, bowling, easy walking, golf)	_____

9. Describe briefly your typical weekly physical exercise. Indicate approximate duration frequency and intensity. For example: " I jog 3 miles, 2 times per week at 10 minute per mile." or "I walk every day, about a mile", or "no regular exercise":

_____
_____
_____

10. Would you be apprehensive or concerned for your health if you were asked to walk for 20 minutes without stopping? □ Yes □ No

APPENDIX 3 – Recruitment Flyer

Do You Have Peripheral Arterial Disease?

UNC is Studying Mobility in People with Peripheral Arterial Disease

The Applied Biomechanics Lab at UNC Chapel Hill is looking for volunteers to take part in a research study to test whether a simple new exercise device that promotes ankle rotation can improve exercise tolerance and walking ability in people with peripheral arterial disease. The experiment involves some walking and biking tests, and some seated ankle exercises while having your body motion and muscle activity recorded. All experiments are completely non-invasive and have been approved by the University of North Carolina at Chapel Hill Institutional Review Board. To take part you must:

- Be age 65 years or older
- Be free of orthopedic injury
- Be able to walk comfortably without an assistive aid (e.g. walker, cane)
- Have peripheral arterial disease

Experiments will consist of visiting our lab twice up to 3 hours each. Some participants will be invited to take part in an ankle exercise intervention. Subjects will be compensated for their time.

For more information, please contact:
Jason Franz
Department of Biomedical Engineering
UNCABLstudies@unc.edu (Phone: 919-445-2331)