Low Risk Protocol

Project Title

The effect of Niagara® Cycloid® action on legs with chronic oedema/lymphoedema following treatment for cancer

Project team

Principal Investigator responsible for activity at site

Name: Prof Neil Piller	**Qualifications**: BSc (hons) Ph D, FACP
Lead site and Department: Lymphoedema Clinical Research Unit, College of Medicine and Public Health, Flinders University	
What is the position of this person on the research project? Principal Investigator	
What are the research activities this person will be responsible for: Study oversight; Study oversight; Consenting; Trial planning, support of the team during measurements, participant communication, taking some measurements (PERO and BIS when needed) cross checking of input data. **Does this person have a current Good Clinical Practice certificate that you will submit with your application?** ☒ Yes / ☐ No - Good Clinical Practice training is required by all listed investigators, as per National Clinical Trials Governance Framework action 1.2 and 1.6	
Contact details: **a Health or University email address is preferred** ☐ **I am the contact person for this project**	**Phone**: 82044711 **Email**: neil.piller@flinders.edu.au

Associate Investigators – add additional tables or rows for all researchers involved in the study

Name: Richard Allan	
Site and Department: : College of Medicine and Public Health, Flinders University	
What is the position of this person on the research project? Investigator (Consultant Vascular Sonographer)	
What are the research activities this person will be responsible for: Ultrasound Doppler data collection/analysis **Does this person have a current Good Clinical Practice certificate that you will submit with your application?** ☒ Yes / ☐ No - Good Clinical Practice training is required by all listed investigators, as per National Clinical Trials Governance Framework action 1.2 and 1.6	
Contact details: a Health or University email address must be used ☐ **I am the contact person for this project**	**Phone**: 8204 6796 **Email:** richard.allan@flinders.edu.au
Name: Marielle Esplin	
Site and Department: : Lymphoedema Clinical Research Unit, College of Medicine and Public Health, Flinders University	

What is the position of this person on the research project? Clinical Research Officer	
What are the research activities this person will be responsible for: Study Coordinator; Ethics submissions, placing advertisements, recruitment, assisting entry of participants into trial, data collection/measurement of parameters in the trial (except those associated with Ultrasound Doppler which will be carried out by a Sonographer), data entry, preparation of data for analysis **Does this person have a current Good Clinical Practice certificate that you will submit with your application?** ☒ Yes / ☐ No - Good Clinical Practice training is required by all listed investigators, as per National Clinical Trials Governance Framework action 1.2 and 1.6	
Contact details: a Health or University email address must be used ☒ **I am the contact person for this project**	**Phone**: 8204 4903 / 0438 357 622 **Email:** marielle.esplin@flinders.edu.au

Research Overview

Please provide a brief overview of the study:

Recruit and conduct a single site randomised controlled crossover clinical trial of the impact of 3 weeks home use of **Niagara® Cycloid®** massage pad action on chronic unilateral chronic oedema/lymphoedema of the legs arising as a consequence of treatment for cancer of the bowel, other abdominal structures (including ovaries and prostrate) and melanoma. There will be a follow up period at 2 weeks and at 1 month. The massage pad is a TGA-approved medical device, class IIa (ARTG 151788).

Background and literature review

Correctly and externally applied vibration is widely regarded as having a potential for bringing about improvements in a range of health disorders and conditions as well as when there are undiagnosed or un-recognised pathologies. Human studies have shown that cycloid vibration therapy (CVT) applied externally to the skin can increase venous and arterial blood flow and the movement of interstitial fluid in people with lymphoedema (swelling caused by abnormal accumulation of lymph fluid). This increased local area blood flow may assist in the reduction of lymphoedema, musculoskeletal pain and improve joint mobility. In turn, improving quality of life and general wellbeing.

The current, albeit sometimes poor-quality evidence, suggests that lower vibration frequencies may be more efficacious however there are a range of frequencies that can be beneficial. Review of recent scientific literature over the last 20 years on the optimum vibration frequencies for a range of disorders and diseases shows there has only been one or two experimental or clinical studies that have a good experimental design, have a reasonable sample size and are controlled. Most of the published studies are without experimental control, are anecdotal or use only a small sample size. The literature shows that the vibrational treatments used are primitive in the application and transmittance of the force and primitive in design, sample selection and rigor. As well, there is limited evidence that the range of frequencies and amplitude and repeat cycling used is anywhere near optimal. Some unrelated work on tissues and cells suggest that other than currently used frequencies, timing and penetration may give much better and more objective results than those currently obtained.

Lymphoedema can occur following cancer treatment when the lymphatic system is damaged through node removal as occurs with cancer surgery or damage as occurs with radiotherapy. The lymphatic system fails when confronted with a continuing load at or above the maximum reserve capacity of the system such as occurs when the lymphatics are chronically overloaded due to infection, high arterial or venous (back) pressures. Conservative estimates indicate at least 20% of cancer survivors develop lymphoedema. In the case of lower limb lymphoedema, this can have substantial negative effects on quality of life, impaired limb function, pain and skin changes.

Since the lymphatic system is a slow system normally pulsating at between 6-10 times per minute at rest, a slow variation in tissue pressure throughout the tissues is critical to best ensure loading of the lymphatics and transport in them. The benefits of such low frequencies have been shown in two major studies conducted by our Unit using the Niagara® Cycloid® massage pad, with 42 hz being optimal (the lowest frequency setting on the device). In regard to the published literature available, we still need a clearer picture of the movement of blood into and out of the limb and treated area, as well as general fluids and materials carried by the tissue fluids and the blood and the movement of fluids within the interstitium via lymphatics distal to proximal. Important also is the movement of blood/fluids into areas in which the fluids already have been removed (that is the more proximal areas).

In respect of optimising outcomes for lymphoedema on the basis of our prior knowledge of the lymphatic system, the massage pad must be applied first proximally and then distally. It must be ensured that the wave pattern is distal to proximal (important for ensuring flow of blood from the limb) utilising the valves in the lymphatic vessels and the flow of fluids. Being cognizant of this importance and given the results of our prior clinical trials, placement of the massage pad in the abdominal, anterior/posterior thigh and calf is recommended. The ability for a single wave to flow over the whole area in contact with the pad but always in a direction towards the root of an extremity or the most distal part of it is a key need of this study. This means correct placement of the pad is crucial and to facilitate this phone-review will be utilised. Linkage of the pad used to the phase of respiration with pressures being higher at the root of the extremity when one is inhaling is important, so we would recommend normal but deep breathing just prior to using the pad and immediately after use (5 breathing cycles so as to be sure this is not a confounder in the trial).

Rationale / justification

The incidence of lymphoedema following cancer treatment is a concern worldwide, affecting quality of life and limb function. There are limited studies available on the benefits vibrational therapy for lymphoedema with scientific rigour. This trial will provide an opportunity for a comprehensive investigation into vibrational therapy and how the vibration influences body tissues and functions on people affected with leg lymphoedema following cancer treatment. This trial includes a control design, with participants measured at the same timings as in the treatment group but conducting their normal lymphoedema care. Participants would be randomly selected into the control group or treatment group and then a cross over design employed. This research will aid in providing data on the effects of vibrational therapy for the maintenance of leg health in those with lymphoedema.

Hypothesis and/or Research Question

That daily 30 minutes of CVT externally applied to a lymphoedematous leg over 3 weeks has an impact on blood flow into and out of the treated limb, influencing limb extracellular fluids and volume.

Aims -

To determine the impact of 30 minutes of daily CVT over 3 weeks on blood flow, fluid content and limb size of legs of participants affected with lymphoedema following cancer treatment.

To determine the efficacy of home delivered CVT on leg lymphoedema following cancer treatment through use of a TGA-approved massage pad.

Objectives -

To better understand the impact of CVT on blood flow into and out of the major vessels of lymphoedematous legs, compared to a normal lymphoedema care

To measure main arterial inflow and venous outflow from the treated and non-treated legs using

ultrasound sonography.

To measure total leg fluid volume changes using Bioimpedance Spectroscopy and Perometry.

To measure skin integrity changes using indurometry.

To measure skin moisture changes of the lower leg using a portable moisture meter.

Expected outcomes -

Change in arterial inflow, venous outflow in the main vessels of the lower limb and a concomitant change in limb size and volume.

Project design

Anticipated start and finish dates: May 2024 (as soon as ethics approval is received) to Nov 2025

Estimated last first participant enrolled: May 2024

Estimated date last participant completed: September 2025

Study Sites/Settings:

- Lymphoedema Clinical Research Unit, Flinders University

Recruitment target:

Estimated sample size of 30 final participants based on our current best knowledge based on prior trials of the pad we have conducted.

Methodology - clearly describe the specific procedures or techniques that will be used to answer the research question and meet the aims.

Participants will be randomly allocated into either the treatment or control group by odd vs even number selection. In the control group, participants will conduct their normal lymphoedema care routine. In the treatment group, the participant's lymphedematous leg will be treated with the Niagara® Cyclopad for a total of 30 minutes (i.e. 10 minutes each in three locations; lower back, upper leg and lower leg) using the set minimum frequency. There will be 5 cycles of deep breathing before and after the massage pad use. Participants will be asked to rest supine for 15 mins prior to starting each treatment. At the end of their 4-week follow-up period, the participant will be crossed over into the other group.

Measurement points are:

- Screen
- Baseline
- Day 1/2 (phone call)
- Day 4
- 1 week
- 2 weeks
- 3 weeks
- 2 weeks Follow-up
- 4 weeks Follow-up

Please see Table 1 for Schedule of assessments.

Procedure	SCREEN	BASELINE	PHONE CALL (Day 1 or 2)	DAY 4	WEEK 1	WEEK 2	WEEK 3	FOLLOW-UP 1 (2 weeks)	FOLLOW-UP 2 (4 weeks)
			Treatment or Control Phase					Post-Treatment/Control Phase	
Visit	1	2	3	4	5	6	7	8	9
Informed Consent	✓								
Eligibility Criteria	✓								
Demographics	✓								
Medical History	✓								
Physical Exam	✓	✓							
Vital Signs	✓	✓		✓	✓	✓	✓	✓	✓
Height	✓	✓							
Weight	✓	✓		✓	✓	✓	✓	✓	✓
LYMQOL		✓					✓	✓	✓
Symptom Scale (10-point Likert)		✓					✓	✓	✓
Bioimpedance	✓	✓		✓	✓	✓	✓	✓	✓
Limb Volume	✓	✓		✓	✓	✓	✓	✓	✓
MoistureMeter D		✓		✓	✓	✓	✓	✓	✓
Tonometry/Skin FibroMeter		✓		✓	✓	✓	✓	✓	✓
Conconmitant Medications	✓	✓		✓	✓	✓	✓	✓	✓
Review Participant use of device in-situ			✓						
Review Participant Diary			✓	✓	✓	✓	✓		
Sonography		✓					✓	✓	

crossover to other group

Procedure	BASELINE	PHONE CALL (Day 1 or 2)	DAY 4	WEEK 1	WEEK 2	WEEK 3	FOLLOW-UP 1 (2 weeks)	FOLLOW-UP 2 (4 weeks)
		Treatment or Control Phase					Post-Treatment/Control Phase	
Visit	10	11	12	13	14	15	16	17
Informed Consent								
Eligibility Criteria								
Demographics								
Medical History								
Physical Exam	✓							
Vital Signs	✓		✓	✓	✓	✓	✓	✓
Height	✓							
Weight	✓		✓	✓	✓	✓	✓	✓
LYMQOL	✓					✓	✓	✓
Symptom Scale (10-point Likert)	✓					✓	✓	✓
Bioimpedance	✓		✓	✓	✓	✓	✓	✓
Limb Volume	✓		✓	✓	✓	✓	✓	✓
MoistureMeter D	✓		✓	✓	✓	✓	✓	✓
Tonometry/Skin FibroMeter	✓		✓	✓	✓	✓	✓	✓
Conconmitant Medications	✓		✓	✓	✓	✓	✓	✓
Review Participant use of device in-situ		✓						
Review Participant Diary		✓	✓	✓	✓	✓		
Sonography	✓					✓	✓	

Table 1 – Schedule of Assessments.

Brief general medical history questionnaire

A brief general medical history questionnaire will be taken at baseline regarding age, current and past illnesses, the nature of the intervention causing the chronic oedema/lymphoedema, number of lymph nodes removed, radio therapy, adjunct therapy, any medications, exercise status and regime and lymphoedema care routine.

Quantitative Data

Height, weight, heart rate, blood pressure will be taken and recorded at each clinic appointment.

At each presentation at the clinic during treatment and follow-up periods, the following measurements will be taken. Assessment will include the standard assessment procedures currently used in the Lymphoedema Clinical Research Unit (they all have prior ethics approval for many trials and are part of normal diagnostic tools):

- Perometry to measure total limb volume
- Bio-impedance Spectroscopy (BIS) for total fluids
- Indurometry measurement in lymphatic territories (3 sites)
- Moisture-meter measurement fluids in lymphatic territories (3 sites)
- Sonography for measurement of blood inflow and outflow and volumes and velocities

Perometry (opto-electronic) measurement to obtain both total leg volumes. This equipment is non-invasive and involves a frame being moved up and down the legs in a period of about 10 seconds. This equipment has been used in all prior trials approved by ethics committee and is in wide use here and around the world to assess total limb volumes and their changes.

Bioimpedance Spectroscopy measurement of both leg fluid volumes. The participant stands on a metal platform and holds hand grips. Time required for this measurement is 1-2 minutes. This is non-invasive and involves the generation of a range of frequencies, which travel through the tissues of the arms and legs. Different tissues/fluids and their contents lead to different impedances to electrical flow leading to an overall body composition reading. Of particular interest are the fluid levels in the extracellular compartments of the legs.

Ultrasound doppler to measure blood flow (used in FMC and other vascular clinics), paying attention to flow volumes and velocities at the location of major femoral vein and artery in each of the lower limbs, near the groin area. This will be performed with participants lying on a bed and take between 3-7 minutes.

Moisture Meter analysis to measure the moisture content in the skin of the legs using a portable device that tests the bioelectric impedance of the skin. It passes a painless and safe electrical current through the skin measuring how long the current takes to travel from one sensor to the other. A determinant of the moisture level of the skin is made.

Indurometery to measure the skin integrity using a portable device that measures how hard the tissue is (tissue's resistance to compression). It is a painless measure of induration of the skin and upper subcutis noninvasively.

Qualitative Data

Symptom Scale (10-point Likert)

Participants will be asked to rate 10 symptoms commonly associated with limb swelling such as tightness, heaviness, cramps, skin dryness burning feelings etc using a 10 point Likert scale. (1 = no problem or issue to 10 = worst imaginable problem or issue).

Quality of Life impact

A Leg LYMQL will be administered prior to and at the end of the treatment and follow-up periods. This is a validated instrument to measure the impact of leg lymphoedema on a patient's quality of life developed by Prof Vaughan Keeley.

Feedback

On Day 1/2 after treatment/placebo, a follow-up phone call will be made by the LCRU staff member to record any feedback regarding of treatment and ascertain proper placement of the pad during treatment. This will be an unstructured open-ended interview.

Participants will be asked to provide any comments about using the massage pad after the 3-week use. This will documented and emergent themes viewed.

Consumer and Community engagement –

The Unit has a close affiliation with the local and national support and advocacy groups. The PI is patron of the national support group Lymphoedema Association Australia and regularly discusses potential studies with these groups.

What are your outcomes for the research and how are they measured?

Measurements are described above in Methodology Section. The outcome will be an improved understanding of the impact of CVT on the blood flow into and out of lymphoedematous legs and of its impact on overall leg and fluid volumes. As well as perceived impact of the participant on symptoms and quality of life and use of the device.

Inclusion criteria –

Clinically diagnosed Chronic oedema/lymphoedema (arising from treatment for cancer) of one leg, more than 1.5 years duration but less than 10 years duration

Age group 45-75,

Male or Female

BMI classes: Overweight 25-29.9 and Obese Class I (Moderately obese) 30-34.9

Exclusion Criteria –

Clinically diagnosed thyroid disorder (nor medications for it)

Venous issues of the legs including venous reflux, significant varicosities or signs of venous disorder/disease (LDS, Haemosiderin in over large areas) Spider veins and minor superficial venous telangiectasia ok)

Leg swelling prior to the intervention for cancer (statement from the referring clinician about this)

Medications likely to have an influence on sodium retention such as Beta blockers, Diuretics

Current wounds/ulcers on the legs

Signs of significant recent soft tissue wounding

Signs of current skin breakdown.

Abnormal liver, renal and heart function

Current or recent (< 1 month) bacterial infections (Cellulitis)

Pregnant

Cardiac pacemaker

large metal plates/implants

Funding

Please provide a brief explanation:

Funding source: Sponsor - Niagara® CT Health Care

Funding amount: $ $11,870.55 per trial participant

Who will manage the study budget? Lymphoedema Clinical Research Unit, Flinders University

Is there additional funding support provided by an external source? No

Storage of blood and/or tissue samples

☒ **Not applicable for this research study**

Consent

How you will be obtaining consent and/or what alternatives you will be using?

Written consent after the provision of the PICF to potential participants. Potential participants will have at least a week to read the PICF and consider the study and discuss with their GP/Family, before then obtaining consent at an appointment. The consenting appointment will allow for time to answer any further questions. This is a low-risk study given non- invasive measurements.

Please advise (by name) which investigators will provide the information sheet and consent form to the participant?

Study Coordinator – Marielle Esplin

Please advise (by name) investigators who will obtain consent?

- Principal Investigator– Prof Neil Piller
- Study Coordinator – Marielle Esplin

How much time will participants have to consider participation?

Potential participants will be given at least one week to consider participation in the study but can take more time if required.

Will there be an opportunity to confirm or renegotiate consent during the research project:

☒ Yes

☐ No

Who will be confirming or renegotiating consent with participants?
Principal Investigator or Study Coordinator

What process will be undertaken and how will participants be supported through this process?
Staff will be available at all times at appointments and via phone call to discuss any participant changes to consent.

Waiver of consent/Pre-screen Waiver of consent

Are you requesting a waiver of consent to pre-screen a data source for the purpose of identifying eligible potential candidates to invite to participate in this study? No

Are you requesting a waiver of consent and no participant information sheet or consent form will be used for this study?

☒ No

☐ Yes - **The waiver of consent must be justified using the National Statement chapter 2.3.9 and 2.3.10**

(a) to (i).

Please:

(a) Demonstrate how involvement in this research carries no more than low risk to participants. Refer to The National Statement chapters 2.1.6 and 2.17 for guidance.

(b) Explain how the benefits from the research justify any risks of harm associated with not seeking consent

(c) Explain why it is impracticable to obtain consent (for example, due to the quantity, age or accessibility of records).

(d) Explain why there is no known or likely reason for thinking that participants would not have consented if they had been asked.

(e) Demonstrate there is sufficient protection of their privacy.

(f) Demonstrate there is an adequate plan to protect the confidentiality of data.

(g) Explain in the case the results have significance for the participant's welfare there is, where practicable, a plan for making information arising from the research available to them i.e. via a disease-specific website or regional news media).

h) Explain the possibility of commercial exploitation of derivatives of the data or tissue will not deprive the participants any financial benefits to which they would have been entitled.

(i) **Demonstrate the waiver is not prohibited by State, Federal or international law.**

Participant selection and activities

How are potential participants identified as suitable for the research?

Advertisement notice attached separately. Participants will be recruited from the local lymphoedema clinics and by word of mouth from those who decided to participate. Advertisement will be placed on relevant notice boards in clinics. All will be provided with the full details (see PICF) if they express verbal interest.

How will participants be recruited into the study?

Potential participants will see advertisement and then on the basis of that decide if they wish to participate. We anticipate some interest by word of mouth and in these cases the potential participant will be provided with the advertisement, followed by the PICF if still interested.

Who is approaching the participants about this research project?

Self-identification through awareness of the ad or Lymphoedema Therapist will notify a potential participant of the study.

When is this occurring?

Clinic – a lymphoedema therapist will notify the potential participant that the trial is available.

Are participants reimbursed for parking, travel or time involved?

☐ No

☒ Yes

Please detail what is being reimbursed and the amount:

Participants will be reimbursed $10 for parking and provided a $10 gift voucher for a light meal or drink at a local café**.** Participants will be able to keep the massage pad provided to them during the trial at the end of the study.

Participant commitment -

Participants will have 17 appointments over the full crossover study design (from screening to 4 week follow-up). Two of these visits will be a phone call (Day 1 or 2). Assessments are non-invasive and outlines in the Methodology Section.

Participant follow up –

Participants have clinic appointments at Screening, Week 1, Week 2, Week 3, 2-week Follow-Up and 4-week Follow-Up (for both the treatment and control arm). There will be a phone call on Day 1 or Day 2 to monitor progress and home use of the massage pad.

Ethical considerations

Please describe the risk and burden associated with your research.

This research is of no risk of harm or discomfort and no risk for minor burden or inconvenience. The only foreseeable risk is no greater than discomfort. The massage pad is a TGA-approved medical device, class IIa (ARTG 151788) and the assessments are non-invasive. There is a risk the quality of life questionnaire (LYMQL) may cause distress. Counselling will be provided if required.

How will any risks be managed?

Participant is free to withdraw from the study if they find the treatment discomforting.

Benefits – please identify and explain the expected outcomes and benefits of the study

The outcome will be an improved understanding of the impact of CVT on the blood flow into and out of lymphoedematous legs and of its impact on overall leg and fluid volumes. As well as perceived impact of the participant on symptoms and quality of life and use of the device.

Does a dependant or unequal relationship exist between the participant and the researcher?

☐ Yes -

How will the dependant / unequal relationship be managed?

☒ No

Conflicts of interest: Please refer to the National Statement chapter 5.4, and your institutional policy for guidance.

☐ Yes / ☒ No

Please provide details of the conflict of interest and how it will be managed:

Data management plan

Which listed investigators will collect the study data / information?

SC will collect all data and enter into an Excel spreadsheet (located on Flinders University password-protected computer drive). Sonographer will collected ultrasound data and SC will enter this into the spreadsheet.

What type of data will be used?

☐ **Data that has never been labelled with individual identifiers or from which identifiers have been permanently removed, and by means of which no specific individual can be identified.**

☐ **Identifiable - data that contains an identifier or combination of identifiers i.e.name, date of birth, image, address, URN**

☒ **Data in which identifiers have been removed and replaced by a code, but it remains possible to re-identify a specific individual by, for example, using the code or linking different data sets.**

If the data being used has the potential to identify a patient, please justify and describe how accidental re-identification will avoided?

Any identifying codes will be removed and replaced by numbers only.

If the participant's medical records are being accessed - please state where the information is being collected

N/A

Data sets -

Ultrasound doppler – flow rates, flow volumes from major artery and veins on both legs, as per the data output from the Doppler unit. This is then transcribed into a excel data sheet.

Perometry - the total volume and circumferences of both limbs are noted from the perometry program and transcribed into the excel data sheet.

Bio-impedance Spectroscopy - Total limb fluids and other body composition characteristics (Total Fluids, Extra cellular and Intra cellular, total muscle and total fats) are noted from the data collection screen and transcribed into the excel data sheet.

Indurometry – value of skin integrity are recorded and transcribed into the excel data sheet.

Symptom Scale (10-point Likert) and LYMQL Questionnaires – score provided will be recorded and transcribed into the excel data sheet.

Feedback – responses will be recorded into the excel data sheet and any themes summarised.

What format will the data or information be stored?

Excel files on Flinders University password protected staff computer.

Please provide details regarding training of the research team on maintaining the integrity and security of the data -

All staff have completed their good clinical practice certificates.
What conditions can the data be accessed or granted to others? For Statistical analysis of de-identified data by statistician
How will the research data be stored and what security measures are in place to protect it during the research? Access by password only on FUSA computer.
How will you provide access to, disclose, use/re-use or transfer the data to other sites? N/A except for statistical analysis of whole data set
How long will the data be retained for? ☐ **The data will be kept for 15 years – for all SA Health research** ☒ **The data will be kept for 5 years – for all University research,**
What plans are in place to store / archive the study data once the research is completed? Hard copy study data will be archived for 5 years in locked compactus in swipe-access Flinders University room. Any data all will be stored on FUSA computer with password access only. **What is the archive plan if the chief investigator leaves the institution and no longer has access to the study data?** Transfer of access of data set to new Flinders Lymphoedema Clinical Research Unit Clinic staff.
How will the study data be destroyed? Any hard copy shredded into confidential waste bins and any electronic data deleted.
Who is responsible for the study data disposal? SC

Analysis

Clearly detail the statistical analysis methods that will be used to meet the study aims and/or test the study hypothesis.

Matching and sampling strategies: Participants will be randomly allocated into either the treatment or control group by odd vs even number selection. After the 4 week follow-up period, the participants will be crossed over into the other group (treatment or control). In the event a participant does not wish to participate in the second group then either another participant who intends to participate in both will be chosen or a second participant chosen with matching bio data (Age, gender, BMI).
Accounting for potential bias, confounding factors and missing information: Randomisation will help avoid bias. We will also be able to observe if there are conditions such as psoriasis, infection etc on the limbs and exclude participants if not declared in initial responses. Missing information is unlikely due to the short time of the intervention and measurement period. Should it occur due to equipment failure then the participant could be invited to return. Failing this the data set would be excluded from the analysis
Sample size and statistical or power issues –

This study is one following information collected from a prior pilot trial and has informed us a sample size of 30 is adequate. While a statistical outcome is useful, we also will examine what we see as "biological" or "practical" changes. However, given the relative homogeneity of the sample and the fact that we do not intend to undertake or rely on any subgroup analysis the sample size of 30 is adequate. The equipment we use i.e., perometry is able to accurately and detect changes in limb volumes of 50ml in a 5000ml limb section and our Bio-impedance analysis unit can detect fluid changes of 10ml per limb.

How will you measure, manipulate and/or analyse the information collected?
All data will be used in its raw form as generated by the measuring equipment. Analysis initially by excel and followed by analysis using STATA or similar statistical program as appropriate.

Data linkage – what linkages are planned or anticipated?
None

Participants may withdraw from the study by choice, what impact will a participant withdrawing have on the data?

Should they withdraw, they will be replaced by another matched participant completely or for the arm of the trial that they withdrew from. Given the massage pad is available on the market and this is low risk research, we don't anticipate many participants to withdraw.

How will this be responded to?

Once the participant has let the research team know that they wish to withdraw, the withdrawal will be documented. If the participant wishes a follow-up on lymphoedema status, this will be conducted. A participant may provide the research team with the reason(s) for leaving the study, but is not required to provide their reason.

Results, reporting, outcomes, and future plans

Please detail your plans for the return of the research results to the participants:
Participants will be given a copy of the data gained from the Perometer, the BIS analyser (giving them details of their BMI, muscle, fats, fluids and a fitness score similar to those given at gyms) at the end of each clinic appointment. They will also be given a copy of the overall study results.

What are your plans for dissemination and publication of project outcomes?

We would intend to present research outcomes at the Australasian Lymphology Association meeting in 2025 as it has relevance to disorders such as lymphoedema and chronic oedema.

Will you be providing a de-identified data set to the journal for verification purposes?

All data collected is de-identified and will have a re-identification code so that the remaining information does not identify an individual.

Please detail other potential uses of the data at the end of the project:

Inform us of what benefits might come from massage pad use in lymphoedema at the base frequency setting.

What are your plans for sharing and/or future use of data and/or follow-up research? i.e., anticipated secondary use of data: If results are publishable and presentable, we plan to share with publications and conferences; including conferences with community engagement. De-identified results will be shared with Sponsor. The results will inform us on the direction of any future research in this area, including if vibration therapy, an easily applied, non-invasive therapy, can optimise outcomes for lymphoedema management. If a benefit is measured, infrared and indocyanine green imaging studies would be considered to detail the response of the lymphatics through location and function before and after treatment, as well as research of the effect of this therapy on other lymphatic conditions.
What is the project closure process? Final HREC report and report to the sponsor. Destruction of the data after 5 years.