Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Sheffield Hallam University

# Information for participants Part 1 (Pilot study)

## The effects of different modes of exercise on microcirculatory parameters in patients with Systemic Sclerosis.

### Introduction

We are inviting you to participate in a research study. Before you decide whether you would like to take part, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with us and/or friends if you wish. If you require more information or any further clarification on the information given to you we will gladly be at your disposal to answer at any relative inquiry. Please take your time to decide whether or not you wish to take part.

### Background and purpose of the study

Approximately 50% of patients with Systemic Sclerosis develop decreased blood flow in the fingers and/or wound which seem to be painful, difficult to heal, susceptible to infections and heavily influences quality of life. Raynaud's phenomenon is a common condition with vasospasm in the small veins and arteries of the fingers causing pallor with cyanosis and/or rubor. It usually consists of painful vascular spasms of the fingers stressed by cold or emotional changes.

Although we know the capability of exercise to improve vascular function (blood flow) in the large arteries in several clinical populations, we still do not know about the effectiveness of exercise in the small arteries in Systemic Sclerosis patients. The mode of exercise (cycling or arm-cranking) may play an important role in improving the blood flow in the small arteries of the fingers in these patients. Hence, the purpose of the study is to examine the effectiveness of exercise through two different modes (cycling and arm-cranking) in Systemic Sclerosis patients.

### Am I suitable participant for the study?

We are recruiting men and women aged 18-80 years old, who are diagnosed with SSc experiencing RP for a period between 1 to 10 years being able to perform the planned exercise programme. Patients will be selected according to their medical profile by our

collaborator physician. Those with cardiovascular disease, other inflammatory condition than Systemic Sclerosis, current smokers or women in pregnancy will not be able to participate. The study can be divided in three phases (Table 1). During the study proceedings you have the right to withdraw at any time you wish to.

**What will happen if I take part?**

If you are eligible for the study and are happy to take part we will arrange for you to attend the Centre for Sport and Exercise Science at Sheffield Hallam University where the baseline measurements will take place (See table 1 below). You will be asked to sign a consent form agreeing to take part in the study. You will be given a copy of your signed consent form and this information sheet to keep.

The study design is a randomised controlled trial which means that you will be allocated to either the exercise groups (cycling or arm-cranking) or to the control group (no exercise) by chance (random).

**Exercise group:** If you are randomised to the exercise groups you will be asked to attend the Centre for Sport and Exercise Science at Sheffield Hallam University twice for the baseline measurements. We will provide you with instructions on how to get to the centre and where you can park for free. Unfortunately we are unable to pay other travel costs. Afterwards, a training period of 12 weeks will commence where you will be required to attend the gym located at the Centre for Sport and Exercise Science at Sheffield Hallam University two times per week to perform a supervised exercise session. Training hours and dates will be fixed according to your eligibility and in agreement with the personal trainer. Straight after the 12-week training period you will be asked to visit our laboratories at the Centre for Sport and Exercise Science at Sheffield Hallam University twice in order to be assessed in the same tests as prior the exercise intervention (post-exercise intervention measurements-see Table 1).

**1st visit:** will include questionnaires that will estimate your quality of life, examination of the small arteries of the fingers (non-invasively), body weight and height and a 6 minute walking test. Here you will be asked to walk up and down a corridor and cover as far a distance as possible in 6 minutes. The 6 minute walking test will give us an essential indication about your functional capacity to perform daily activities. The assessment of the small blood vessels in the skin of your fingers function will be performed using a non-invasive test called

laser Doppler fluximetry. Two small sticky patches will be applied to the skin of your reference finger. Tiny quantities of two drugs will be administered through these patches (no injections), which will cause local relaxation of the small blood vessels in your finger. Special probes and computer software will be used to measure changes in skin blood flow. This procedure will be performed when you are lying down and relaxed.

**2nd visit:** The second visit will take place the next or the next few days after the first visit. It involves an examination of the small arteries of the fingers (non-invasively). Moreover, both groups (exercise and control) will be required to perform a maximal oxygen uptake test where it will be performed either on a cycle ergometer or on an arm crank ergometer. The maximal oxygen uptake test will help us assess your physical fitness, identify reasons related to your disease that might impair your ability to perform exercise and examine the differences before and after the exercise programme on several outcomes.

**The maximal oxygen uptake test:** involves a procedure where a blood pressure cuff will be attached at your arm during the exercise test on a cycle or arm-crank ergometer to assess the blood pressure at various intervals, a mouthpiece will be placed to measure the inhaled and exhaled oxygen breath by breath. We will also place to your chest some pads connected with the electrocardiogram to assess the electrical signs of your heart during exercise. While you exercise the intensity will increase progressively up to a maximal level which will only be sustained for a few minutes. The whole visit will last roughly 30 to 40 minutes and the actual exercise test will last between 8 to 12 minutes.

**Exercise session:** Participants assigned to the exercise groups will be invited to undertake 2 sessions of supervised exercise training each week for 12 consecutive weeks at The Centre for Sport and Exercise Science at Sheffield Hallam University. Each session will last approximately 30-40 minutes and will involve 30 minutes of an aerobic individualized exercise protocol performed either on a cycle ergometer or on arm-crank ergometer accompanied by the warm-up (5 minutes) and cool down (5 minutes) period. Patients assigned to the control group will receive basic advice about exercise but no supervised training.

During some of the exercise sessions you will be required to fill in questionnaires relating to your affect and enjoyment of the each protocol and type of exercise. Moreover, a sub-sample of six participants will be randomly chosen from each group in order to be interviewed. The

interview will refer to your experience of Raynaud's phenomenon, treatment and advice given, your preference for trial allocation (exercise or control group) as well as your experiences of study participation in both the exercise groups and the control group. You will meet with the researcher face to face at the end of the exercise intervention for about 30-35 minutes.

Before the baseline measurements participants will be randomly allocated into three groups (Group A- exercise group, Group B-exercise group and Group C-control group).

Some participants will be randomly invited to take part in the interview after completing the final exercise session so we can explore your experiences of the exercise programme and study.

**Control Group:** If you are randomised to the control group you will be asked to attend the Centre for Sport and Exercise Science at Sheffield Hallam University for all the measurements but will not take part in the exercise intervention. Between the baseline measurements and those after 12 weeks you will be receiving regular calls, approximately once a week, to obtain information about your condition.

Whichever group you are in you will keep taking your normal medical treatment that has been prescribed by your physician for the digital pain you experience.

All the visits will take place at the Centre for Sport and Exercise Science at Sheffield Hallam University.

Table 1: Overview of the study

| Visit number | Purpose of visit | Duration of visit |
|---|---|---|
| 1 | **Baseline measurements**<br>Quality of life questionnaires, laser-doppler fluximetry assessments,<br>body weight and height, 6min walking test | 60 minutes |

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| 2 | **Baseline measurements**<br>Laser-doppler fluximetry assessment,<br>maximal oxygen uptake test on cycle or arm ergometer **(8-12 minutes)**. | 60 minutes |
| 3-26 | **Training sessions (exercise groups only)**<br>• 2 sessions per week<br>• 30 minutes aerobic exercise either on cycle or arm-crank ergometer | 35-40 minutes |
| 27 | **Post-exercise intervention measurements**<br>Quality of life questionnaires, laser-doppler fluximetry assessments,<br>body composition, 6-MWT. | 90 minutes |
| 28 | **Post-exercise intervention measurements**<br>Maximal oxygen uptake test on cycle or arm ergometer **(8-12 minutes)**, interview. | 60 minutes |

**What do I have to do?**

Before the baseline and post-exercise intervention measurements you will be requested to abstain from vigorous exercise, alcohol, caffeine and tobacco for a period of 24h but also to be at least 2h fasting prior to the assessment as these parameters could affect your responses. We encourage you to wear sport clothing that will allow for a more comfortable movement during the exercise test.

**What are the possible benefits of taking part in this study?**

This study is being undertaken for research purposes and to advance our knowledge in the mode of exercise that will potentially improve the blood flow in the small arteries of the fingers. It is not known whether exercise will make the condition better, however, people who undertake regular exercise training often become fitter and healthier but also previous research has shown that exercise can improve blood flow in the larger arteries of the body, so you might experience this if you are allocated to the exercise group.

**What happens if something goes wrong?**

All of the experimental procedures that will be used in this study have been rigorously tested to ensure that they meet health and safety standards. These tests are all routinely and regularly performed on patients and healthy volunteers alike. The researchers who perform the tests are all trained and skilled to do so. If we notice any signs, as regards your health status, that may cause you harm by participating, you will be informed and withdrawn immediately from the study.

Overall the risks of the procedures included in this study are low. The potential risks associated with the microvascular assessments include skin irritation and infection and will be minimised through strict adherence to established protocols, using sterile procedures and carefully prepared pharmacological agents. These sessions will be conducted by appropriately-trained staff.

**What if I change my mind during the study?**

You are free to withdraw from the study at any time. If you decide to withdraw, we may ask you to consider attending one final assessment, but this is entirely optional. You can choose to leave the study at any time without having any further assessments. We would like to use all of your data up to the point of withdrawal as this will help with our analysis. However, if you would prefer us not to use any of your data you may request for all of your data to be removed from the study. A decision not to carry on with the study will not affect the quality of care you receive in any way.

**Will taking in this study be kept confidential?**

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically at Sheffield Hallam University under the provisions of the 1998 Data Protection Act. Your name will not be passed to anyone else outside the research team or the sponsor, who is not involved in the trial. You will be allocated a trial number, which will be used as a code to identify you on all trial forms.

The information collected about you may also be shown to authorised people from the UK Regulatory Authority, the local NHS Trust and Independent Ethics Committee; this is to ensure that the study is carried out to the highest possible scientific standards. All the study research team will have a duty of confidentiality to you as a research participant.

If you withdraw consent from further study involvement, unless you object, your data will remain on file and will be included in the final study analysis.

In line with Good Clinical Practice guidelines, at the end of the study, your data will be securely archived for a minimum of 7 years from the end of the study (the end of the study is defined as the last visit of the last patient in the study). Arrangements for confidential destruction will then be made.

Coded results from the study may be stored indefinitely for subsequent analyses in the future. Any identifying information is kept strictly confidential, and access will be limited strictly to the original study team and database team. Researchers analysing the clinical data in the future will be unable to identify you.

With your permission, your GP, and other doctors who may be treating you, will be notified that you are taking part in this study.

**Who will be working on the study?**

The researcher in charge is Mr. Alexandros Mitropoulos (PhD student in Clinical Exercise Physiology), supervised by Dr. Markos Klonizakis (Senior Research Fellow in Clinical Physiology) and the leading NHS clinician collaborating to the study is Dr. Mohammed Akil (Consultant Rheumatologist).

**What will happen to the results of the study?**

Once the study has been completed all data will be anonymised and stored as per current data protection laws. The results will be written up for publication in academic journals and possibly used at academic conferences and will also contribute to a Doctor of Philosophy degree (PhD) completion. Anything with your personal details (name, DOB, contact details etc.) will be kept securely in a locked filing cabinet by the Principal Investigator. Overall study results will also be made available to you on request at the end of the study. Moreover, information provided by the participant will be stored at Sheffield Hallam Research Facilities in Sheffield for further analyses until the end of the project.

**What if I have further questions or would like more information about the study?**

If you would like more information about the study you are invited to contact:-

Mr. Alexandros Mitropoulos, Sheffield Hallam University tel. 07926126426.

**What happens if I have a complaint?**

If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study. If you have complaints on concerns please contact the project co-ordinator Dr. Markos Klonizakis Tel 0114 225 5697. Or alternately you can use the normal Trust complaints procedure and contact PALS Advisor, Social Care NHS Foundation Trust, Tel 0114 275 8956. If you require an independent individual to complain about this study through Sheffield Hallam University, you may contact Dr. Donna Woodhouse (Senior Lecturer) Chair Sport Exercise Research Ethics Group and Vice Chair Faculty Research Ethics Committee via email d.woodhouse@shu.ac.uk or by telephone on 0114 225 5670 or by letter Academy of Sport and Physical Activity, Faculty of Health & Wellbeing, Sheffield Hallam University, A225 Collegiate Hall, Collegiate Crescent, Sheffield, South Yorkshire, S10 2BP.

**What if I am harmed?**

In the event that something does go wrong and you are harmed during the research study, there are no special compensation arrangements. If you are harmed as a result of someone's negligence then you may have grounds for legal action for compensation, but you may have to pay your legal costs.

**Who is organizing and funding the research?**

This study is being funded by the Sheffield Hallam University and supported by the Sheffield Teaching Hospitals NHS Trsut. The investigators of this study will not receive any payment for conducting this research.

**Who has reviewed the study?**

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed by London - West London & GTAC Research Ethics Committee, NHS.

**Further information/independent advice**

If you require any further information or independent advice about this study, please contact the Patient Advice And Liaison Service (PALS) Team Monday-Friday 9am-5pm by telephone on 0114 271 8956, via email on complaints@shsc.nhs.uk or in person at the Patient Advice And Liaison Service (PALS), Fulwood House, Old Fulwood Road, Sheffield, South Yorkshire (by appointment).

**Thank you for taking the time to read this information sheet and to consider this study.**

**Study Team Contact Details**

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Collegiate Hall, Collegiate Campus, Sheffield, S10 2BP.

**Researcher:**

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