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Camera monitoring of circulation dynamics using skin perfusion pattern of lower limbs

Submission date	**Recruitment status**	[X] Prospectively registered
17/07/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
15/08/2019	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
15/06/2020	Circulatory System	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Maintaining adequate perfusion of blood and nutrients to all regions of the body is a key aim for all clinicians, but perfusion is difficult to measure directly. Many indirect whole-body measures are used such as blood pressure. In clinical settings, examination of the skin provides useful information about whole-body perfusion. Clinical examination is known to add more to the overall assessment of a patient's clinical state than just the vital sign measurements. Skin blood flow in healthy individuals varies from almost nothing to up to 60% of the heart's output of blood depending on the circumstances. In situations of circulatory collapse, the body's response is to cut down the amount of blood supplying the skin and redirect them to the more vital areas. This change can be detected on examination as pale (or mottled/marbled appearance of skin) and cool skin, but may also be detected by video cameras. The researchers have previously designed and ran a healthy volunteer study to develop non-invasive and non-contact measurement of blood flow velocity to reflect the underlying circulation. The changes measured by the video camera agreed with the changes detected by conventional methods of monitoring. One of the other findings from this previous study was that the timing and pattern of arrival of pulse/blood flow to different regions of skin does not follow what is known about the anatomical distribution of the larger blood vessels. The sequence by which the skin is perfused is not known, and it is not known whether a general pattern exists which agrees person-to-person. An understanding of this normal pattern may be key to developing a tool which can detect changes in underlying blood flow/heart function by detecting changes in this pattern.

Who can participate?
Healthy men and women aged 18 to 65

What does the study involve?
The normal pattern of blood perfusion is assessed in terms of the sequence and distribution of blood arrival. The researchers will then create changes by giving drugs which will increase and decrease the diameter of blood vessels near the surface of the skin. They will describe the directional changes in perfusion pattern created by these opposite-acting drugs. In the second part of the experiment, the researchers will place a tourniquet to temporarily stop the blood flow into the legs. After 60 seconds, they will deflate the tourniquet and study the sequence in which blood re-fills the leg vessels. This will give an idea of the underlying connection of blood

vessels and help create a map of the normal blood perfusion pattern. The study visit will take about 2 hours.

What are the possible benefits and risks of participating?
The participants will be given a £50 voucher for participation. In terms of risks, the participants may experience discomfort during insertion of the drip which will remain in place for the duration of camera recording. The two drugs being used are safe and have been used in heart research in healthy volunteers at higher doses than the researchers intend to use, but may cause increase or decrease in blood pressure, headaches, and breathlessness. In order to minimise the risks, the researchers will be monitoring the participants closely and a dedicated doctor will be present for safety of the participants.

Where is the study run from?
Cardiovascular Clinical Research Facility in the John Radcliffe Hospital, Oxford (UK)

When is the study starting and how long is it expected to run for?
March 2019 to September 2023

Who is funding the study?
Oxford Biomedical Research Centre (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
R63796/RE001

Study information

Scientific Title
Optical monitoring of changes in perfusion map of lower limbs compared to traditional haemodynamic monitoring methods in response to pharmacological challenges in healthy volunteers or Mapping Of Lower Limb skIn pErfusion (MOLLIE)

Acronym
MOLLIE

Study objectives
1. Changes in peripheral circulation induced by phenylephrine and glyceryl trinitrate can be detected by video-based monitors by tracking changes in the perfusion map of lower limbs (where perfusion map is the chronological order of pulsatile signal arrival to different regions of interest of lower limb skin).
2. Changes in peripheral circulation induced by phenylephrine and glyceryl trinitrate can be detected by video-based monitors by tracking changes in the temperature map of lower limbs.
3. Changes in pulsatile signal of lower limb regions of interest can be used to identify arterial perforator locations.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/07/2019, Medical Sciences Interdivisional Research Ethics Committee (Research Services, University of Oxford, Wellington Square, Oxford, OX1 2JD, UK; Tel: +44 (0)1865 616577; Email: ethics@medsci.ox.ac.uk), ref: R63796/RE001

Study design
Single-centre non-randomised study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Perfusion of lower limbs

Interventions
1. Infusion of phenylephrine to induce peripheral vasoconstriction
2. Infusion of glyceryl trinitrate (GTN) to induce peripheral vasoconstriction
3. Tourniquet application to lower limb followed by tourniquet release

The aim of this study is to describe the normal pattern of blood perfusion in terms of the sequence and distribution of blood arrival. The researchers will then create changes in the

cardiovascular state by giving drugs which will increase and decrease the diameter of blood vessels near the surface of the skin. They will describe the directional changes in perfusion pattern created by these opposite-acting drugs.

In the second part of the experiment, the researchers will place a tourniquet to temporarily stop the blood flow into the legs. After 60 seconds, they will deflate the tourniquet and study the sequence in which blood re-fills the leg vessels. This will give an idea of the underlying connection of blood vessels and help create a map of the normal blood perfusion pattern.

Proposed timeline:
00:00 – 00:10 Consent check, measure height/weight/skin colour
00:10 – 00:20 History and examination
00:20 – 00:30 IV cannulation, IV infusion set up
00:30 – 00:40 Positioning in bed, check equipment set up (trial recording), set up reference devices
00:40 Recording starts
00:40 – 00:50 Rest period with no intervention
00:50 – 01:05 15-minute infusion drug 1
01:05 – 01:35 20-minute Washout period
01:35 – 01:50 15-minute infusion drug 2
01:50 – 02:20 20-minute Washout period
02:20 – 02:25 Tourniquet inflation and release
02:25 End of study
Post study: final check, medical review prior to leaving

Intervention Type
Other

Primary outcome(s)
Skin perfusion pattern at rest and change to the pattern post-exposure to phenylephrine and glyceryl trinitrate (GTN). Measured using composite measures from three different cameras measuring in visible, near-infrared, and infrared spectrum. Measures taken will include the strength of pulsatile signal measured at skin surface, absolute skin colour change when under constant lighting and angle, skin surface temperature gradient from proximal to distal areas, blood flow measurement using laser speckle contrast imager. Measurements will be taken at baseline, at one-minute intervals with increasing dose of phenylephrine and GTN, and at stable infusion maximal dose.

Key secondary outcome(s))
Current secondary outcome measures as of 17/02/2020:
1. Pulse transit time between proximal and distal regions of interest estimated from the photoplethysmographic signal using the camera set up as described for the primary outcome measure at baseline, at one-minute intervals with increasing dose of phenylephrine and GTN, and at stable infusion maximal dose
2. Surface temperature gradient between proximal and distal regions of interest measured using the camera set up as described for the primary outcome measure at baseline, at one-minute intervals with increasing dose of phenylephrine and GTN, and at stable infusion maximal dose
3. Proportions of visible skin surface with pulsatile photoplethysmographic component measured using the camera set up as described for the primary outcome measure at baseline, at one-minute intervals with increasing dose of phenylephrine and GTN, and at stable infusion maximal dose

4. Colour changes with increasing phenylephrine and GTN infusion measured using the camera set up as described for the primary outcome measure at baseline, at one-minute intervals with increasing dose of phenylephrine and GTN, and at stable infusion maximal dose
5. Description of the chronological order of skin perfusion when the lower limb is reperfused following the application and removal of a lower limb tourniquet, measured using the camera set up as described for the primary outcome measure continuously during the planned one-minute tourniquet application and in the 5 minutes following tourniquet release

Previous secondary outcome measures:
Chronological order of skin perfusion when lower limb is reperfused following application and removal of a lower limb tourniquet. Measured using the same camera set up as primary outcome measure, across all exposed regions of skin of lower limb (from mid-thigh to mid-shin). Measurements will be taken continuously during the one-minute tourniquet application and in the 5 minutes following tourniquet release.

Completion date
30/09/2023

Eligibility

Key inclusion criteria
Healthy males and females between the ages of 18 to 65

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patient whose anatomy, condition, or other required monitoring precludes the use of the camera equipment or thoracic bioimpedance monitor kit. Examples include skin disorders such as eczema, scleroderma or psoriasis
2. Allergy to silver chloride ECG sensors
3. Hyperthyroidism (intravenous phenylephrine contraindicated)
4. Any regular medication except combined oral contraceptives
5. Pregnant or breastfeeding
6. History or current psychiatric illness
7. History or current neurological conditions (e.g. epilepsy)
8. History of cardiovascular disease making phenylephrine or GTN unsafe

Date of first enrolment
01/10/2019

Date of final enrolment
31/05/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cardiovascular Clinical Research Facility
John Radcliffe Hospital
Headley Way
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research organisation

Funder Name
Oxford Biomedical Research Centre

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available as the data from the camera cannot be completely anonymised. In the ethics application this was extensively discussed and it was decided that the dataset will be held in a secure setting behind two doors and restricted access within Kadoorie Centre for Critical Care Research and Education and Institute of Biomedical Engineering secure server.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	11/06/2020	15/06/2020	Yes	No