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# Topical Oxygen and Diabetic Foot Ulcers 2

**Submission date**
02/02/2015

**Recruitment status**
No longer recruiting

**Registration date**
08/06/2015

**Overall study status**
Completed

**Last Edited**
07/01/2019

**Condition category**
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Many wounds fail to heal because of inadequate oxygen levels. Diabetic foot wounds that fail to heal place their sufferers at risk of amputation. The most widespread method of increasing oxygen delivery to wounds to date has been the use of hyperbaric chambers for wounds where there is poor perfusion. These are expensive and time consuming with potential side effects and complications and their use is not common in Europe. The Natrox™ system is a device designed to overcome a number of problems associated with previous methods of oxygen therapy, by delivering continuous oxygen to the wound bed through a dressing. It consists of a small rechargable battery-powered oxygen concentrator which processes oxygen from air and which because of its size and weight is portable and can be held in place by a lightweight strap. It has a very high level of acceptability with patients. A previous study showed that over an 8-week period there was a reduction of around 50% in the size of some chronic hard to heal diabetic foot wounds. This study will contribute to the understanding of the management of these wounds by reviewing the reductions in wound size achieved using Natrox™ topical oxygen therapy. As well as confirming whether the device is clinically effective, we will also study its cost-effectiveness.

Who can participate?
Male and female patients aged 18 or over with a diabetic foot ulcer.

What does the study involve?
Participants that have had diabetic foot ulcers from between 4 week and 6 months are randomly allocated into one of two groups. Those in group 1 (intervention) are treated with the Natrox™ system in addition to conventional diabetic ulcer dressing. Those participants in group 2 (control) are treated with a device that looks identical to the Natrox™ device, but does not work. The dressings are changed every 2-3 days and the patietns are followed up on a weekly or fornightly basis to assess how well they are feeling, pain they are experiencing, their general quality of life and whether they are suffering from any adverse effects. Participants that have had their diabetic foot ulcers for longer than 6 months are all given the Natrox™ treatment and are followed up in the same way as the intervention group.

What are the possible benefits and risks of participating?
The treatment may be effective in aiding wound healing but this has not yet been tested formally. There is a risk that the treatment may be of no benefit.

Where is the study run from?
Hospitals run by 12 NHS trusts in the UK

When is the study starting and how long is it expected to run for?
December 2014 to September 2018

Who is funding the study?
Papworth Hospital NHS Foundation Trust (UK)

Who is the main contact?
Mr Paul Hayes

# Contact information

### Type(s)
Public

### Contact name
Dr Paul Hayes

### Contact details
Dept of Vascular Surgery
Addenbrookes Hospital
Cambridge
United Kingdom
CB2 0QQ

# Additional identifiers

### EudraCT/CTIS number

### IRAS number
166923

### ClinicalTrials.gov number

### Secondary identifying numbers
1.0 19/12/2014, IRAS project ID: 166923

# Study information

### Scientific Title
A randomised, double-blind, placebo-controlled multi-center trial, examining the effect of Topical Oxygen (Natrox TM) on the rates of healing for chronic Diabetic Foot Ulcers 2 (TODFU-2)

### Acronym
TODFU-2

## Study objectives
Applying additional topical oxygen to chronic diabetic foot wounds will increase the rate of wound healing after 12 weeks of therapy.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
NRES Committee East Midlands - Leicester, 09/01/2015, ref: 15/EM/0021

## Study design
Double-blinded randomised controlled trial

## Primary study design
Interventional

## Secondary study design
Randomised cross over trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

## Health condition(s) or problem(s) studied
Patients with diabetic foot ulcers present for more than 4 weeks

## Interventions
All subjects who are screened will be divided into two groups.

Group 1 – subjects with diabetic foot ulcers between 4 weeks and 6 months
Subjects are blinded into two arms – active treatment and placebo. The active treatment arm receives the actual Natrox device by having it applied over the surface of the wound, in addition to conventional diabetic ulcer dressing. The placebo arm receives a device that looks identical but is non-functional, and has it applied to the ulcer in the same manner, again in addition to conventional dressing. The dressings are changed every 2-3 days and followed up on a weekly or fortnightly basis over 12 weeks, to assess healing, pain, quality of life and any adverse events. Unblinding occurs if the ulcer has healed less than 20% of the baseline wound size, and given the option to cross over to the treatment arm if they were receiving the placebo, or to withdraw from the study. These patients, including those that heal greater than 20%, are followed up over another 12 weeks or until the ulcer heals.

Group 2 – subjects with diabetic foot ulcers greater than 6 months
Subjects are all given the active treatment and followed up as per the treatment arm of group 1

## Intervention Type

Device

### Primary outcome measure
Reduction in wound size at 12 weeks relative to the baseline measurement

### Secondary outcome measures
1. Absolute closure numbers during the 24-week follow-up period
2. Wound closure rate on a per protocol basis during the 24-week follow-up period
3. Number of infective episodes during the 24-week follow-up period
4. Number of dressing episodes during the 24-week follow-up period
5. Days of hospital treatment as a result of DFU complications after date of randomisation (extra data collection if hospitalised) during the 24-week follow-up period
6. QoL (diabetic foot ulcer scale) at the baseline visit and visits 1 to 8, 10, 12 and 14, and at the 24-week follow-up visit
7. Pain as reported by a visual analogue score at the baseline visit and visits 1 to 8, 10, 12 and 14, and 24-week follow-up

### Overall study start date
08/12/2014

### Completion date
30/09/2018

## Eligibility

### Key inclusion criteria
1. A diabetic foot ulcer greater than 4 weeks and less than 6 months in duration for group 1 and gr

2. Minor amputation sites < 50% healed in 4 weeks (the use of negative pressure wound therapy to

3. 2 weeks of standard of care at the hospital based diabetic foot clinic or in a specialist community

clinic prior to randomisation or entry into the open registry
4. No planned future revascularisation (endovascular or open surgery) or randomisation within 4 w

revascularisation being performed
5. Ongoing active chemical or sharp wound debridement prior to, and during, the application of Na

6. No limit on level of ischaemia, either high or low.
The extent of arterial disease will be documented by angiogram or
duplex ultrasound and toe blood pressure.
The extent of the disease will be documented using the Bollinger score.
7. The subject is 18 years of age or older
8. The patient is willing to complete >75% of follow--
up evaluations required by the study protocol
9. The patient is able to abstain from any other treatment of the ulcer for the duration of the study

10. The patient agrees to abstain from enrolment in any other clinical trial for the duration of the s

11. The patient is able to read and understand instructions and give voluntary written informed cor

12. The patient is able and willing to follow the protocol requirements

## Participant type(s)
Patient

## Age group
Adult

## Lower age limit
18 Years

## Sex
Both

## Target number of participants
140

## Key exclusion criteria
1. Inability to comply with dressing regime or manage the Natrox™ device
2. Absolute need for a total contact cast
3. Disseminated malignancy
4. Subjects with a life expectancy <1 year
5. Subjects with an ulcer which is <0.5 cm2 or >50 cm2
6. Subject who is dialysis dependent
7. The subject has an invasive soft tissue infection at the time of baseline assessment, requiring or

8. Exposed bone without soft tissue or granulation tissue across the surface
9. Acute osteomyelitis (stable, chronic osteomyelitis is allowable, including those maintained on or

10. Subject being treated with immunosuppressive medication greater than 7.5
mg prednisolone daily
11. Pregnant/lactating females (selfreported or tested, per institutional requirements)
12. Glycated haemoglobin HbA1C of >12mmol mol-1
13. Subjects who have evidence of connective tissue disorders (e.
g., vasculitis or rheumatoid arthritis) under active treatment
14. The subject is unable to follow the protocol
15. The subject has other concurrent conditions that in the opinion of the investigator may compro

16. The patient is a vulnerable or protected adult
17. The patient is unable to provide consent
18. DFU connected to a sinus wound
19. Wounds were it is felt clinically necessary to cover the surface in gel or creams that would prev

## Date of first enrolment
01/03/2015

## Date of final enrolment
01/08/2015

# Locations

**Countries of recruitment**
England

Scotland

United Kingdom

**Study participating centre**
**Cambridge University Hospitals**
United Kingdom
CB2 0QQ

**Study participating centre**
**St Georges's Healthcare NHS Trust**
United Kingdom
SW17 0QT

**Study participating centre**
**Southampton University Hospitals NHS Trust**
United Kingdom
SO16 6YD

**Study participating centre**
**North Bristol NHS Trust**
United Kingdom
BS10 5NB

**Study participating centre**
**King's College Hospital NHS Foundation Trust**
United Kingdom
SE5 9RS

**Study participating centre**
**Heart of England NHS Foundation Trust**
United Kingdom
B9 5ST

**Study participating centre**
**The Newcastle upon Tyne Hospitals NHS Foundation Trust**
United Kingdom
NE7 7DN

**Study participating centre**
**Cardiff University Wound Healing Research Centre**
United Kingdom
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**Study participating centre**
**Edinburgh Royal Infirmary**
United Kingdom
EH16 4SA

**Study participating centre**
**University Hospitals of Leicester NHS Trust**
United Kingdom
LE5 4QF

**Study participating centre**
**Leeds Teaching Hospitals NHS Trust**
United Kingdom
LS1 3EX

**Study participating centre**
**Imperial College Healthcare NHS Trust**
United Kingdom
W2 1NY

# Sponsor information

**Organisation**
Inotec AMD

### Sponsor details
Butts Business Centre
Royston
United Kingdom
SG8 7SL

### Sponsor type
Industry

### Website
http://www.inotecamd.com/contact-us

## Funder(s)

### Funder type
Hospital/treatment centre

### Funder Name
Papworth Hospital NHS Foundation Trust (UK)

## Results and Publications

### Publication and dissemination plan
The data will be analysed once the trial is complete, and this is likely to be in Feb 2016. The plan is to produce at least 3 papers, one on the clinical impact of the RCT, one on the associated registry, and a final one on the potential cost-effectiveness of the intervention. The journals will be chosen according to the potential impact of the results. We also plan to present the data at national and international meetings, if accepted for presentation or poster sessions.

Updated 07/01/2019:
Peer-reviewed papers will be published separately for the Group 1 and Group 2 studies. A paper on the Group 2 results is currently under preparation. Analysis of the much more complex Group 1 data has commenced, with submission for publication envisaged during 2019.

### Intention to publish date
31/12/2019

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. The study results comprise, for each of the two Groups separately, multiple large datasets covering patient parameters, responses to treatment, and (for Group 1) randomisation details. The core datasets are libraries of photographs, which poses additional privacy concerns. These datasets will be maintained and archived in digital form, together with a paper-based Trial Master File, by the sponsor, Inotec AMD Limited. In addition, individual study sites will each archive their source data and study records in defined archiving facilities.

## IPD sharing plan summary

Not expected to be made available

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Abstract results | preliminary results in conference proceedings | 01/09/2017 | | No | No |
| HRA research summary | | | 28/06/2023 | No | No |