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Remote ischaemic Conditioning After Stroke Trial - 3

Submission date
06/02/2020

Recruitment status
Recruiting

Registration date
20/04/2020

Overall study status
Ongoing

Last Edited
09/04/2025

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Strokes are very common with ~100 000 strokes occurring every year in the UK. The majority (80%) are caused by a blocked blood vessel and others are caused by a ruptured blood vessel. There are very few treatments for strokes, such as using medicines or wires to unblock blood vessels, but they can only be used in a small proportion of strokes caused by blocked blood vessels.
A treatment called 'remote ischaemic conditioning' (RIC) could help protect the brain from damage caused by stroke. RIC is performed by inflating a blood pressure cuff on the arm, briefly interrupting its blood supply; the cuff is deflated after 5 minutes and repeated 4 times. The process causes body chemicals to be released into the bloodstream which have a protective effect on the brain and may reduce the size of the stroke and reduce disability – this has been shown in experimental models of stroke but the treatment has not been proven in humans.

We have completed a small trial of 26 stroke patients (called RECAST-1) who used RIC soon after their stroke - RIC was very well tolerated and caused minimal side effects. We have also completed a second trial (RECAST-2) of 60 stroke patients showing we can perform RIC urgently within 6 hours of new stroke symptoms. The trial has also suggested that RIC may be able to prevent ongoing damage caused by stroke.

We plan to perform a trial across 60 UK hospitals including 1300 stroke patients called RECAST-3. Half of the participants will receive RIC, and the other half will have a sham procedure performed (a placebo). Patients will be identified and invited to take part in the trial by the Stroke Team as soon as they arrive in the hospital. The participants will have a 50:50 chance of receiving RIC or the sham procedure. RIC or sham is performed twice a day for up to 14 days (28 doses). Consent can be given by a relative or carer if the patient is not able to give it themselves. This will occur at the same time as routine treatments (such as receiving clot-busting medicine). The participant will be invited to take part in other parts of the study, including additional brain scans looking at the size of the stroke and blood tests (measuring blood proteins). The participant will be seen again by the research team on the 14th day after recruitment into the trial to answer questions on the trial treatment. After discharge from the hospital, the participant will be contacted over the telephone 3 months later to answer questions about their physical ability, mood, memory and quality of life.

New treatments will likely have their greatest effect if administered in the first few hours after a stroke. RIC is an attractive potential treatment since it would be simple and cheap to administer by medics, other healthcare professionals (nurses, paramedics) or even non-medically trained personnel. If this study shows that RIC is beneficial in reducing stroke recurrence and leading to a lower level of disability, it would have significant social, medical and financial benefits to patients, families and society.

Who can participate?
Patients at one of the participating hospitals who have a diagnosis of an ischaemic (blocked blood vessel) stroke. Patients who are over 18 years old and within 48 hours of their stroke starting will be included.

What does the study involve?
Patients who have been diagnosed with a stroke will be recruited to the study in the hospital.

Participants will either receive a treatment called 'remote ischaemic conditioning' (RIC) or a sham treatment. RIC is performed by inflating bilateral blood pressure cuffs on both arms, briefly interrupting the blood supply; the cuffs are deflated after 5 minutes and repeated 4 times. Participants will receive this treatment up to 28 times within 14 days of the onset of their stroke.

Participants will be assessed by doctors while in the hospital and will have a follow-up assessment by telephone call after 90 days.

What are the possible benefits and risks of participating?
We cannot promise the study will help participants but it might help reduce how badly the current stroke affects participants or it might reduce the chances of having another stroke. The information we get from this study will help in deciding the best treatments for future stroke patients.

The main disadvantage is that participants may experience some discomfort when the blood pressure cuff is kept inflated. There is a small risk that prolonged cuff inflation could cause bruising or bleeding under the skin of the participant's arm and this will be monitored closely.

Participants in the study may have a second CT brain scan on day 2, which is arranged as part of their routine care depending on the treatment already received. This procedure uses ionising radiation to form images of the head and provide the doctor with clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their lives. Standard care scans performed whilst taking part in this study will increase the chances of this happening to participants from 50% to 50.02%.

Where is the study run from?
The study is run by the University of Nottingham (UK) and will take place at 60 hospitals in the UK

When is the study starting and how long is it expected to run for?
From April 2020 to September 2026

Who is funding the study?
The National Institute for Health Research (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
277021

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
20011, CPMS 44839, IRAS 277021

Study information

Scientific Title
Remote Ischaemic Conditioning After Stroke Trial (ReCAST- 3)

Acronym
ReCAST-3

Study objectives
Remote ischaemic perconditioning (RIC) is safe and improves functional outcome in patients presenting with hyperacute stroke.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 27/05/2020, Greater Manchester (GM) South Health Research Authority (Barlow House, 4 Minshull St, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8221; gmsouth.rec@hra.nhs.uk), ref: 20/NW/0173

2. approved 11/06/2020, Scotland A Research Ethics Committee (2nd Floor Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 (0)131 465 5680; manx.neill@nhslothian.scot.nhs.uk), ref: 20/SS/0047

Study design
Phase III prospective randomized (1:1) sham-controlled blinded-endpoint parallel-group multicentre trial

Primary study design
Interventional

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Adults with acute ischaemic stroke presenting in Emergency Departments and Stroke Units in the UK

Interventions

Current interventions as of 09/04/2025:
Participants will be allocated to either receive the intervention or the comparator.

The intervention/remote ischaemic conditioning group will receive 4 cycles of intermittent limb ischaemia, alternating 5 mins inflation (+20 mmHg above systolic BP) followed by 5 mins deflation of bilateral automated upper arm blood pressure cuffs.

The comparator/sham remote ischaemic conditioning group will receive 4 cycles of bilateral automated upper arm blood pressure cuffs inflated to 50 mmHg for 5 mins, followed by 5 mins deflation.

For both groups, the first dose will be given within < 48 h of onset, and the second dose will be given if time allows in the day. This will be repeated twice daily for up to 14 days (28 doses).

All participants will be followed up via telephone call at 90 days, blinded to treatment allocation.

Previous interventions as of 20/12/2023 to 09/04/2025:
Participants will be allocated to either receive the intervention or the comparator.

The intervention/remote ischaemic conditioning group will receive 4 cycles of intermittent limb ischaemia, alternating 5 mins inflation (+20 mmHg above systolic BP) followed by 5 mins deflation of bilateral automated upper arm blood pressure cuffs.

The comparator/sham remote ischaemic conditioning group will receive 4 cycles of bilateral automated upper arm blood pressure cuffs inflated to 20 mmHg for 5 mins followed by 5 mins deflation.

For both groups, the first dose will be given within < 24 h of onset, the second dose will be given 6 h after the first dose. This will be repeated twice daily until the end of day 14 for total 28 doses.

All participants will be followed up via telephone call at 90 days blinded to treatment allocation.

Previous interventions:
Participants will be allocated to either receive the intervention or the comparator.

The intervention/remote ischaemic conditioning group will receive 4 cycles of intermittent limb ischaemia, alternating 5 mins inflation (+20 mmHg above systolic BP) followed by 5 mins deflation of an automated upper arm blood pressure cuff.

The comparator/sham remote ischaemic conditioning group will receive 4 cycles of an automated upper arm blood pressure cuff inflated to 20 mmHg for 5 mins followed by 5 mins deflation.

For both groups, the first dose will be given within < 6 h of onset, the second dose will be given 1-2 h after the first dose. This will be repeated twice daily until the end of day 2 for total 4 doses.

All participants will be followed up via telephone call at 90 days blinded to treatment allocation.

Intervention Type

Device

Phase
Phase III

Drug/device/biological/vaccine name(s)
AT4 Tourniquet (AneticAid)

Primary outcome(s)
Death or dependency assessed by the modified Rankin Scale (mRS) ordinal shift analysis recorded using central blinded telephone follow-up at 90 days.

Key secondary outcome(s))
1. Adverse events including: death, neurological deterioration, intracranial haemorrhage, systemic embolism, and other serious adverse events measured through clinical assessment at 2 and 4 days, patient notes at discharge, and responses to central blinded telephone follow-up at 90 days
2. Cerebrovascular events measured through clinical assessment at 2 and 4 days, patient notes at discharge, and responses to central blinded telephone follow-up at 90 days
3. Major adverse cardiac and cerebral events measured through clinical assessment at 2 and 4 days, patient notes at discharge, and responses to central blinded telephone follow-up at 90 days
4. Acute kidney injury measured through clinical assessment at 2 and 4 days, patient notes at discharge, and responses to central blinded telephone follow-up at 90 days
5. Disability measured through responses to central blinded telephone follow-up at 90 days
6. Cognition measured through responses to central blinded telephone follow-up at 90 days
7. Mood measured through responses to central blinded telephone follow-up at 90 days
8. Frailty measured through responses to central blinded telephone follow-up at 90 days
9. Quality of life measured through responses to central blinded telephone follow-up at 90 days

Completion date
30/09/2026

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 09/04/2025:
1. Acute ischaemic stroke
2. <48 h post stroke onset
3. Primary intracerebral haemorrhage ruled out on baseline clinical neuroimaging
4. NIHSS score of 4-25 at randomisation
5. Aged 18 years or above

Previous participant inclusion criteria as of 20/12/2023 to 09/04/2025:
1. Hyperacute ischaemic stroke
2. <24 h post stroke onset
3. Primary intracerebral haemorrhage ruled out on baseline clinical neuroimaging
4. NIHSS score of 5-25 at randomisation
5. Aged 18 years or above

Previous participant inclusion criteria as of 29/04/2020 to 20/12/2023:
1. Hyperacute ischaemic stroke
2. <6 h post stroke onset

3. Primary intracerebral haemorrhage ruled out on baseline clinical neuroimaging
4. NIHSS score of greater than 3 at randomisation
5. Aged 18 years or above

Previous participant inclusion criteria:
1. Hyperacute ischaemic stroke
2. <6 h post stroke onset
3. Primary intracerebral haemorrhage ruled out on baseline clinical neuroimaging
4. NIHSS score >4 at randomisation
5. Aged >18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current participant exclusion criteria as of 09/04/2025:
1. Pre-morbid dependency (modified Rankin Scale, mRS>3)
2. Systolic BP ≤80 mmHg
3. Spontaneous intracerebral haemorrhage
4. Haemorrhagic transformation of infarction PH2 if known before randomisation (not excluded or withdrawn if occurs after randomisation)
5. Dementia - if the patient had a pre-existing diagnosis
6. Coma (GCS <8)
7. Malignancy and significant co-morbidity (life expectancy <6 months)
8. BM <3.0 mmol/L
9. Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia
10. Taking part in another interventional trial, unless co-enrolment has been approved by both Chief Investigators and Sponsors
11. Known pregnancy
12. Significant tissue injury or pre-existing condition of the upper limbs, which in the opinion of the investigator, will be exacerbated by RIC
13. Expected repatriation [within 72 hours] to another hospital not participating in RECAST-3

Previous participant exclusion criteria as of 20/12/2023 to 09/04/2025:
1. Pre-morbid dependency (modified Rankin Scale, mRS>3)
2. Systolic BP ≤80 mmHg
3. Spontaneous intracerebral haemorrhage
4. Haemorrhagic transformation of infarction PH2 if known before randomisation (not excluded or withdrawn if occurs after randomisation)

5. Dementia - if the patient had a pre-existing diagnosis
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8. BM <3.0 mmol/L
9. Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia
10. Taking part in another interventional trial, unless co-enrolment has been approved by both Chief Investigators and Sponsors
11. Known pregnancy
12. Significant tissue injury of the upper limbs, which in the opinion of the investigator, will be exacerbated by RIC
13. Expected repatriation to another hospital not participating in RECAST-3

Previous participant exclusion criteria as of 15/12/2021 to 20/12/2023:
1. Pre-morbid dependency (modified Rankin Scale, mRS>3)
2. Spontaneous intracerebral haemorrhage
3. Haemorrhagic transformation of infarction PH2
4. Dementia
5. Coma (GCS <8)
6. Malignancy and significant co-morbidity (life expectancy <6 months)
7. BM <3.0 mmol/L
8. Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia
9. Taking part in another interventional trial, unless co-enrolment has been approved by both Chief Investigators and Sponsors
10. Known pregnancy

Previous participant exclusion criteria as of 29/04/2020:
1. Pre-morbid dependency (modified Rankin Scale, mRS> 3)
2. Spontaneous intracerebral haemorrhage
3. Dementia
4. Coma (GCS < 8)
5. Malignancy
6. Significant co-morbidity (life expectancy < 6 months)
7. BM < 3.0 mmol/L
8. Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia
9. Known pregnancy

Previous participant exclusion criteria:
1. Pre-morbid dependency (modified Rankin Scale, mRS> 3)
2. Spontaneous intracerebral haemorrhage
3. Dementia
4. Coma (GCS < 8)
5. Malignancy
6. Significant co-morbidity (life expectancy < 6 months)
7. BM < 3.0 mmol/L
8. Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia
9. Long term (> 7 days) nitrate therapy
10. Receiving treatment for diabetes
11. Pregnancy

Date of first enrolment
01/01/2024

Date of final enrolment
30/09/2026

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Yeovil District Hospital
Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre
Watford General Hospital
Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
Luton and Dunstable University Hospital
Lewsey Road
Luton
United Kingdom
LU4 0DZ

Study participating centre
Kent and Canterbury Hospital
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Study participating centre
Queen's Medical Centre
Derby Rd
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Royal Preston Hospital
Sharoe Green Lane

Preston
United Kingdom
NG5 1PB

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Aberdeen Royal Infirmary
Fosterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Queen Elizabeth Medical Centre
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Countess of Chester Hospital
Liverpool Rd
Chester
United Kingdom
CH2 1UL

Study participating centre
Doncaster Royal Infirmary
Armthorpe Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Bronglais General Hospital
Caradoc Road
Aberystwyth
United Kingdom
SY23 1ER

Study participating centre
Prince Philip Hospital
Bryngwyn Mawr
Llanelli
United Kingdom
SA14 8QF

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Cwmrhydyceirw, Swansea
United Kingdom
SA6 6NL

Study participating centre
Glangwili Hospital
Dolgwili Rd
Carmarthen
United Kingdom
SA31 2AF

Study participating centre
Princess Royal Hospital
Farnborough Common
Orpington
United Kingdom
BR6 8ND

Study participating centre
James Cook University Hospital
Marton Rd
Middlesborough
United Kingdom
TS4 3BW

Study participating centre
Royal Stoke University Hospital
Newcastle Rd
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Queen Elizabeth Hospital
Gayton Rd
King's Lynn
United Kingdom
PE30 4ET

Study participating centre
Royal Devon & Exeter Hospital
Barrack Rd

Exeter
United Kingdom
EX2 5DW

Study participating centre
Salford Royal Hospital
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
University College Hospital
235 Euston Road
London
United Kingdom
NW1 2BU

Study participating centre
St. George's Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Dorset County Hospital
Dorset County Hospital
Williams Avenue
Dorchester
United Kingdom
DT1 2JY

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Leighton Hospital
Leighton
Crewe
United Kingdom
CW1 4QJ

Study participating centre
Northumbria Specialist Emergency Care Hospital
Northumbria Way
Cramlington
United Kingdom
NE23 6NZ

Study participating centre
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
University Hospital Monklands
Monkscourt Avenue
Airdrie
United Kingdom
ML6 0JS

Study participating centre
Fairfield General Hospital
Fairfield General Hospital
Rochdale Old Road
Bury

United Kingdom
BL9 7TD

Study participating centre
Russells Hall Hospital
Pensnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
Epsom General Hospital
Dorking Road
Epsom
United Kingdom
KT18 7EG

Study participating centre
The Royal Berkshire Hospital
London Rd
Reading
United Kingdom
RG1 5AN

Study participating centre
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Not defined

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
All data will be stored on a secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one way encryption method). Data will only be available to trial coordinating staff during the trial. Data used for publication will be anonymised.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes