The University of Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

JOINTLY FUNDED BY

Medical Research Council

NIHR | National Institute for Health and Care Research

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

RECAST-3: A multicentre randomised controlled trial

Chief Investigator: Professor Tim England

Professor of Stroke Medicine, University of Nottingham

Honorary Consultant Stroke Physician, Royal Derby Hospital

Email: recast-3@nottingham.ac.uk

Website: https://stroke.nottingham.ac.uk/recast-3/

Twitter: @recast3trial

Telephone: 0115 823 1770

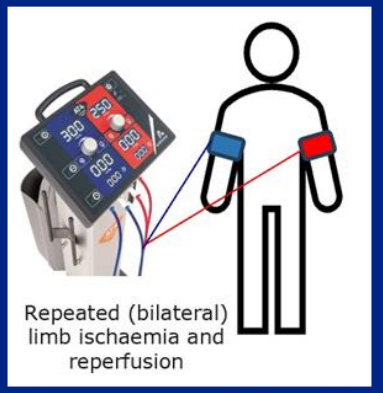
RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

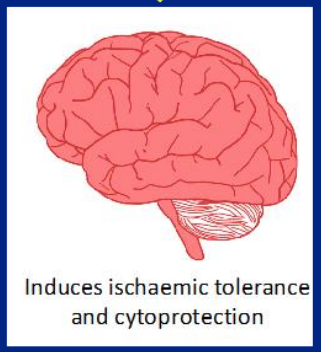
REMOTE ISCHAEMIC CONDITIONING (RIC)

- Remote ischaemic per-conditioning (RIC) in experimental ischaemic stroke is neuroprotective and may reduce ischaemic reperfusion injury.
- It is simply achieved by repeated transient occlusion of the blood supply to a limb using a blood pressure cuff.
- RIC uses repeated cycles of transient limb ischaemia and reperfusion and helps protect the brain from ischaemic reperfusion injury (IRI) through the release of neuroprotective neuro-humoral chemical messengers from the limb, resulting in immediate (first 2-3 hours) and late (24-72 hours) windows of protection from ongoing and delayed cerebral IRI.
- RIC is an attractive strategy since it bears minimal cost, should be safe and would be simple to administer by medics and allied health professionals

Studies to date suggest that further research is required to establish whether RIC improves post-stroke recovery



Release of neuro-humoral mediators



RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

STUDY DESIGN & PURPOSE

PURPOSE: To perform a multicentre randomised controlled trial assessing remote ischaemic conditioning (RIC) in patients with acute ischaemic stroke

- Prospective, randomised, sham-controlled, blinded-endpoint, parallel-group multicentre trial of RIC versus control.
- 1,300 patients with acute (within *24 hours) ischaemic stroke
- Randomised 1:1 across 60 UK based NHS Trusts
- Around 21 patients per site across 29 months of recruitment [60sites]

Amendment to change inclusion time window to ≤48 hours is pending approvals

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

INTERVENTION

- **Active**: RIC group
  - 4 cycles of intermittent bilateral limb ischaemia - alternating 5 minutes inflation (+20 mmHg above systolic BP) followed by 5 minutes deflation of bilateral upper arm BP cuffs.
- **Control**: Sham RIC
  - 4 cycles alternating 5 minutes inflation (to 50 mmHg) followed by 5 minutes deflation of bilateral upper arm BP cuffs.

RECAST-3 Device : CE marked AT4 Electronic Tourniquet, supplied by Anetic Aid Ltd

- **Duration**
  - First 'dose' (4 cycles) *≤24 hours of onset.
  - Second dose on day one if time allows.
  - Twice daily (am/pm) for up to 14 days/28 doses

Please visit our stand (A16) for a demonstration of the AT4 device

Amendment to change inclusion time window to ≤48 hours is pending approvals

Recruitment target:
1-2 per site per month

RECAST 3
REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

Sites open (n=20)
Participants (n=43)
(Up to 28/11/2024)

SITES & RECRUITMENT UPDATE

Open sites (20):

Site	Participants
Royal Derby Hospital	11
Queen's Medical Centre, Nottingham	2
Fairfield General Hospital, Bury	0
Aberdeen Royal Infirmary	1
UCLH	15
Morriston Hospital, Swansea	1
Bronglais General Hospital, Aberystwyth	0
Bradford Royal Infirmary	1
Southampton General Hospital	1
James Cook University Hospital, Middlesbrough	1
Salford Royal Hospital	0
Leighton Hospital, Crewe	3
Charing Cross, London	1
Leicester Royal Infirmary	2
King's College Hospital, London	2
Princess Royal University Hospital, London	0
St. George's Hospital, London	1
Royal Stoke University Hospital	1
Sunderland Royal Hospital	0
Southend University Hospital	0

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

UPCOMING AMENDMENT: MAIN TRIAL

Planned amendment currently in preparation for the main trial:

- Change to eligibility criteria
  - NIHSS change from 5-25 to 4-25
  - Stroke onset change from ≤24 hours to ≤48 hours
  - Change from a minimum delivery of 4 doses to 2 doses as a requirement to be able to 'miss' weekend doses.
  - More pragmatic approach regarding daily dose timings. A couple of hours will be recommended to allow the participant to rest between doses. However, this can be modified, if the participant is willing, to allow two doses to be delivered in one day.
- SAE reporting
  - Change from 20 days to 28 days (to accommodate treatment period that could be up to 23 days to accommodate recruitment late on day 1, missed treatments on weekends/ bank holidays)

We will keep sites updated on the progress of the amendment

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

UPCOMING AMENDMENT: MECHANICAL THROMBECTOMY SUB-STUDY

- The sub-study will be run at selected sites that routinely perform CT perfusion as standard of care at baseline
- Participants will need to be randomised and receive mechanical thrombectomy ≤24 hours post onset

NB:- The upcoming amendment will extend the recruitment window to ≤48 hours for the main trial only

- Scan requirements:
  - Baseline CT head
  - Baseline CT perfusion
  - Day 2 CT head

All standard of care

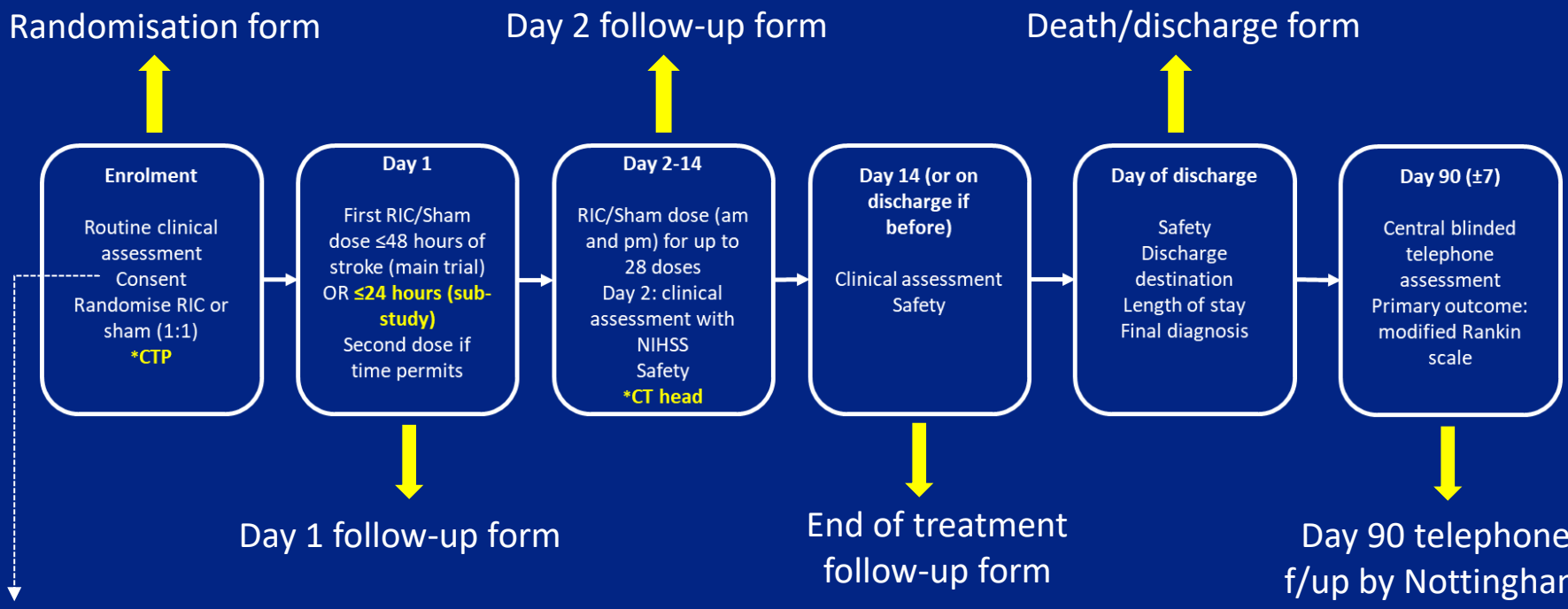
- Sites will be asked to provide data relating to the baseline and follow up scans, and to upload the images and reports (as per the main trial).

We will keep sites updated on the progress of the amendment
Please let us know if your site would be interested in taking part in the sub-study

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

PLANNED POST-AMENDMENT STUDY FLOW



To facilitate recruitment within the therapeutic time window:

- ✓ Non-medics can obtain consent
- ✓ Oral consent followed up with written consent
- ✓ Remote consent
- ✓ Independent physician consent (n/a for Scottish sites)

SCANS:

- Baseline CT scan prior to enrolment
- Baseline CTP scan (*MT sub-study only)
- Day 2 CT head (*MT sub-study only)

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

OTHER UPDATES/REMINDERS

Follow up neuroimaging requirements:

- For all clinical follow up neuroimaging completed after the baseline scan, please complete details of the first follow up CT or MRI scan (if applicable) on the end of treatment CRF (item G1) and upload a copy of the report (to the secure vault) and images (to the database).
- Images and reports for subsequent clinical scans completed until day 90 should also be uploaded.

Neuroimaging report uploads to the secure vault:

- Please ensure that scan reports uploaded to the secure vault are pseudonymised – the date and time should be documented and the participant ID added prior to upload.

Participants consented but not randomised:

- Should a patient be consented but not randomised, we still need a copy of their consent form.
- Please call or email the Coordinating Centre should this happen and we will advise on how to send the consent form to us securely (please don't send this via email to the RECAST-3 mailbox)

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

ACKNOWLEDGEMENTS

RECAST-3 would not be possible without all of the participants and their families that agree to take part in the trial

Thank you also to the RECAST-3 site investigators, co-applicants, trial steering committee, data monitoring committee, funders, Stroke Trials Unit Nottingham and Nottingham Clinical Trials Unit

The University of Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

Thank you!

JOINTLY FUNDED BY

UKRI Medical Research Council

NIHR | National Institute for Health and Care Research

RECAST 3

REMOTE ISCHAEMIC CONDITIONING AFTER STROKE TRIAL 3

ANY QUESTIONS?

WE ARE STILL LOOKING FOR ADDITIONAL SITES TO TAKE PART IN THE RECAST-3 TRIAL

For any further information, or to submit an expression of interest, please contact us at recast-3@nottingham.ac.uk

Email: recast-3@nottingham.ac.uk

Website: https://stroke.nottingham.ac.uk/recast-3/

Twitter: @recast3trial

Telephone: 0115 823 1770