ISRCTN50433077 https://doi.org/10.1186/ISRCTN50433077

Cryoneurolysis to treat pain in the context of spasticity

Submission date
09/09/2025

Recruitment status
Not yet recruiting

Registration date
09/12/2025

Overall study status
Ongoing

Last Edited
07/10/2026

Condition category
Nervous System Diseases

[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
Spasticity is an umbrella term for impairments of muscle activity and control in people with damage to the brain and spinal cord. It is common and results in pain, stiffness, limb deformities, and contributes to difficulties in activities of daily living. Current treatment options, such as stretching, splinting, and Botulinum Toxin injections, are limited, many people experience only partial reduction in spasticity and frequent repeated treatments are needed.
Cryoneurolysis is a medical technique which involves the controlled freezing and thawing of nerves. It has been approved in the UK for the treatment of pain in the context of spasticity through the targeting of nerves which control problematic muscles. Oxford University Hospitals NHS Foundation Trust has been offering this treatment routinely since January 2024. This pilot study aims to improve our understanding of the potential effectiveness of this treatment and its potential side effects when compared with a more commonly used treatment (Botulinum Toxin).

Who can participate?
Adults aged 18 or older who have a central nervous system condition such as brain injury (from stroke, trauma, or bleeding), multiple sclerosis, or spinal cord injury can take part. They need to have spasticity-related pain that is suitable for treatment with Botulinum Toxin and cryoneurolysis, and they should have shown a clear benefit from a diagnostic nerve block. They must have at least one rehabilitation goal focused on reducing pain caused by spasticity.

What does the study involve?
Participants will be randomly allocated to receive usual care with Botulinum Toxin (control group) or usual care with Cryoneurolysis (intervention group). We will assess pain, goal attainment, side effects, spasticity, disability and independence in daily activities, and movement of the arm and leg. Assessments will be at baseline and then 6-, 12-, 18-, and 24-weeks following treatment. Participants who are randomised to the control group will have the opportunity to receive cryoneurolysis treatment after the 12 week follow up assessment.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Oxford University Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
April 2027 to November 2027

Who is funding the study?
Pacira BioSciences (USA)

Who is the main contact?
Dr Anton Pick, Anton.Pick@ouh.nhs.uk

Contact information

Type(s)
Scientific, Principal investigator, Public

Contact name
Dr Anton Pick

Contact details
Oxford Centre for Enablement, Windmill Road
Oxford
United Kingdom
OX3 7HE
+44 (0)1865 737306
anton.pick@ouh.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
1011743

Protocol serial number
CTA 21439/0250/001-0001

Protocol serial number
PID18403

Study information

Scientific Title
Individualised Cryoneurolysis to treat pain in the context of spasticity in the upper and lower Extremities: a pilot randomised controlled trial

Acronym
ICE Trial

Study objectives

Within the context of treating spasticity arising from central neurological conditions, this study's primary objective it to ascertain variability in goal attainment following cryoneurolysis (in addition to usual care) compared to Botulinum Toxin (in addition to usual care).

Secondary objectives:
- To assess pain and potential side effects following cryoneurolysis compared to Botulinum Toxin
- To test for maintenance of effects of cryoneurolysis compared to Botulinum Toxin (between group comparison)
- To test the effects of cryoneurolysis on measures of spasticity, quality and life, and function compared to Botulinum Toxin

Exploratory objectives:
- To explore patient satisfaction, experience, and anticipated barriers/facilitators to clinical implementation
- To explore the potential maintenance of effect of cryoneurolysis (within group comparison)
-To explore the effects of cryoneurolysis compared to Botulinum Toxin (within group comparison)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/12/2025, Wales REC 1 (Health and Care Research Wales, Floor 4, Crown Building, Cardiff, CF10 3NQ, United Kingdom; -; Wales.REC1@wales.nhs.uk), ref: 25/WA/0286

Primary study design
Interventional

Study design
Randomized controlled open-label parallel-group crossover study

Study type(s)
Safety, Other

Health condition(s) or problem(s) studied
Medical condition: Central neurological condition, including acquired brain injury (e.g. from ischaemic stroke, trauma, or haemorrhage), multiple sclerosis, and spinal cord injury.
Medical condition in lay language: Condition affecting the brain or spinal cord
Therapeutic areas: Diseases [C] - Nervous System Diseases [C10]

Interventions
Randomisation (to cryoneurolysis or control, in 1:1 ratio) will be undertaken by the trial team (Trial coordinator or CI) following baseline, using freely available online randomisation software (rando.la). Randomisation includes minimisation between: diagnosis, sex, time since injury /diagnosis, predominant passive or active goals, and requiring treatment of upper/lower limb /both.
Cryoneurolysis: Nerves that require treatment, and the number of treatments required for each nerve will be identified by routine clinical judgement. Nerve targets are identified using an ultrasound machine. The handheld Iovera cryoneurolysis device will be used for treatment. Participants will receive up to 4 treatments of cryoneurolysis for each nerve or nerve branch that requires treatment. It is anticipated that participants will have between 1 and 5 nerves or nerve

branches per limb treated. Each Cryoneurolysis treatment takes 110 seconds. Total treatment time will be determined by number of nerves targeted and number of cryoneurolysis treatments per nerve. The shortest duration, with setup, is likely to be 60 minutes and the longest 120 minutes.
Botulinum toxin: Muscles that require treatment with Botulinum Toxin will be identified by routine clinical assessment. Muscle targets will be identified using an ultrasound machine. It is anticipated that participants will have between 2 and 8 muscles identified for target. The participant will receive up to 200 units of Xeomin (Botulinum Toxin) per muscle that requires treatment. Treatment session of Botulinum Toxin will take 60 to 90 minutes.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
botulinum toxin [Botulinum toxin type A]

Primary outcome(s)
Variability in goal attainment assessed using the Goal Attainment Scale at 6-weeks post-treatment

Key secondary outcome(s)
1. Pain using a numerical rating scale (1–10), DN4, NPSI, and pressure pain thresholds (PPT) — all standard measures, carried out at 6, 12, 18, and 24 weeks.
2. Self-report side effect questionnaire; free-text answers to questionnaire, taken at 6, 12, 18, and 24 weeks.
3. Goal Attainment Scale, standard rating scale at 12, 18, and 24 weeks.
4. Modified Ashworth Scale, standard clinical scale at 6, 12, 18, and 24 weeks.
5. Modified Tardieu Scale, standard clinical scale at 6, 12, 18, and 24 weeks.
6. Spasticity directly assessed by measuring muscle activity to a passive stretch, clinically at 6, 12, 18, and 24 weeks.
7. Range of Motion, standard testing using a goniometer at 6, 12, 18, and 24 weeks.
8. Patient Reported Impact of Spasticity Measure, standard outcome measure at 6, 12, 18, and 24 weeks.
9. EQ-5D, standard measure at 6, 12, 18, and 24 weeks.
10. Spasticity Related Quality of Life instrument (SQoL-6D), standard measure at 6, 12, 18, and 24 weeks.
11. Barthel Index, standard measure at 6, 12, 18, and 24 weeks.
12. Gait assessment, standard assessment in gait lab at 6 and 12 weeks.
13. Leg Activity Measure (LEG-A), standard measure at 6 and 12 weeks.
14. Shriners Hospital Upper Extremity Evaluation (SHUEE), standard measure at 6 and 12 weeks.
15. Arm Activity Measure (ARM-A), standard measure at 6 and 12 weeks.
16. Functional Assessment Test for Upper Limb (FAST-UL), standard measure at 6 and 12 weeks.
17. Questionnaire/interview (exploring patient satisfaction, experience, barriers, and facilitators) at 24 weeks only.

Completion date
01/11/2027

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the trial OR a positive opinion from a consultee is provided by a family member or carer (relative or friend) willing to provide personal consultee (PC) advice.
2. Male or Female, aged 18 years or above.
3. Diagnosed with a central neurological condition, including acquired brain injury (e.g. from ischaemic stroke, trauma, or haemorrhage), multiple sclerosis, and spinal cord injury.
4. Clinical indication for Botulinum Toxin and Cryoneurolysis treatment, including pain associated with spasticity and with a clinically meaningful response to diagnostic nerve block to specific nerves or nerve branches that can be treated with cryoneurolysis.
5. At least one rehabilitation goal related to the management of pain resulting from spasticity.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
99 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Participant has received Botulinum toxin or cryoneurolysis within the last 90 days
2. Raynaud’s syndrome
3. Cryoglobulinaemia
4. Cold urticaria
5. Bleeding disorders
6. Prescribed, or taking antibiotics from the aminoglycoside family
7. Localised infection at the intended treatment site
8. Planned oral antispasmodic medication dose changes
9. Pregnancy, breastfeeding, or planning pregnancy in the trial period
10. Scheduled elective surgery or other procedures requiring general anaesthesia during the trial.
11. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant’s ability to participate in the trial.

12. Participants who are currently enrolled in another trial may be excluded if it is deemed (in the investigator's opinion) that participation could influence the results for either study.

Date of first enrolment
01/04/2027

Date of final enrolment
01/09/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
Nuffield Orthopaedic Centre
Oxford Centre for Enablement
Windmill Road
Headington
Oxford
England
OX3 7HE

Sponsor information

Organisation
Oxford University Hospitals NHS Trust

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Industry

Funder Name
Pacira BioSciences

Alternative Name(s)
Pacira BioSciences, Inc., Pacira, Pacira BioSciences Inc, Pacira BioSciences Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Anton Pick, anton.pick@ouh.nhs.uk, and with a data sharing agreement. Only fully anonymised data will be provided and only upon a reasonable request made by email.

IPD sharing plan summary
Available on request