ISRCTN94245451 https://doi.org/10.1186/ISRCTN94245451

Pre-operative electrical stimulation in carpal tunnel syndrome

Submission date
13/03/2024

Recruitment status
No longer recruiting

Registration date
18/03/2024

Overall study status
Completed

Last Edited
06/01/2026

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
This study is about improving people's recovery after surgery for carpal tunnel syndrome. Carpal tunnel syndrome is a hand disease, in which a nerve becomes compressed at the wrist. This nerve is called the median nerve. The median nerve controls the muscles of the thumb and carries sensation for much of the hand. Compression of the median nerve leads to pain, tingling and weakness in the hand. Carpal tunnel syndrome is common, affecting as many as one in ten people. Most of these people will go on to require wrist surgery to decompress the nerve. However, as many as one in four people still get symptoms after their surgery. We want to explore a new treatment which could improve the results of the surgery. This treatment uses electric pulses to stimulate the median nerve before the operation. We know that electric pulses can help nerves heal after surgery, but currently this treatment requires implanting electrodes in the wrist. Implanting electrodes makes the operation longer, riskier, and more complicated. This study is about electrically stimulating nerves through the skin (non-invasively) instead, to avoid these problems.

Who can participate?
Adults aged 18 years old and over from a specialist hand surgery centre in Oxford, who have been diagnosed with carpal tunnel syndrome and have a decompression operation planned.

What does this study involve?
People with carpal tunnel syndrome who are scheduled for surgery will receive one hour of either real or placebo stimulation around one week before their operation. Everyone will still get the gold-standard surgery. Information will be collected on hand and nerve function before surgery, and then at three months and six months afterwards.

The study team are most interested in seeing if the treatment improves the feeling in people's hands after surgery. However, electrical stimulation is a new therapy and there may be other benefits. To explore this possibility, several other measures of nerve recovery are included. These include tests of whether people's ability to use their hands has improved and measures that allow the team to look more directly at how the nerve is healing. Samples will be taken of skin from the finger and MRI scans of the wrist will be performed before and after surgery, to look at nerves growing back into the skin and recovering from damage. If there are any

differences in these measures between the stimulation and the placebo groups, it will help the team know what to look for in future studies.

What are the possible benefits and risks of participating?
Potential benefits include more rapid and/or more complete sensory, motor and/or functional recovery after surgery. Participants should not be exposed to any additional risks. Stimulation itself poses no risk of long-term harm.

Where is the study run from?
The University of Oxford and the Nuffield Orthopaedic Centre, part of Oxford University Hospitals (UK)

When is the study starting and how long is it expected to run for?
October 2022 to August 2026

Who is funding the study?
1. Medical Research Council (MRC) (UK)
2. British Society for Surgery of the Hand (UK)
3. National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Dr Max Stewart, mdiv1708@ox.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Max Stewart

Contact details
Botnar Research Centre
Oxford
United Kingdom
OX3 7LD
+44 (0)1865 227374
mdiv1708@ox.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
328027

Central Portfolio Management System (CPMS)
60557

Study information

Scientific Title

A single-centre, randomised, parallel-group, double-blinded placebo-controlled study to compare the impact of non-invasive pre-operative electrical stimulation versus placebo on nerve regeneration following decompression surgery for carpal tunnel syndrome

Acronym
PROSpeCT

Study objectives
We hypothesise that 60 minutes of electrical stimulation delivered to the median nerve one week before decompression surgery will accelerate and/or enhance clinical and biological measures of recovery in carpal tunnel syndrome patients

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/03/2024, South Central - Oxford A Research Ethics Committee (Temple Quay House 2 The Square Bristol, Bristol, BS1 6PN, United Kingdom; +44 (0)207 1048171; oxforda.rec@hrs.nhs.uk), ref: 24/SC/0036

Primary study design
Interventional

Study design
Parallel-group randomized controlled patient and outcome assessor-blinded trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Carpal tunnel syndrome scheduled to undergo primary surgical decompression

Interventions
PROSpeCT is a ‘randomised, patient-, surgeon- & assessor-blinded, placebo-controlled clinical trial’. This study design has been chosen as it will best allow us to determine whether the treatment makes a difference to patients.

The study is 'randomised' in that participants will be divided into two groups using computer software. Which group participants end up in is due to chance, or ‘random’, though groups will be balanced for disease severity. Both groups will still receive the current gold standard treatment for carpal tunnel syndrome (carpal tunnel decompression surgery), but only one will get the new electrical stimulation treatment being studied. Randomisation is ‘stratified’ to ensure equal numbers of people with different severities of carpal tunnel syndrome are placed into each group. This approach is used because different severities of carpal tunnel syndrome have different kinds of nerve damage, which could affect response to stimulation.

Placebo-controlled means that while one group will be given the new electrical stimulation treatment and an operation, the other group will be given ‘placebo’ stimulation treatment and their operation. The placebo is a treatment that looks and feels like electrical stimulation but will not affect the nerve’s healing process. Participants will not know which group they are in; hence they are blinded. The researchers measuring outcomes at follow-up will also be blinded.

At the end of the study, results will be compared from the two groups to see if the electrical stimulation produced any improvement.

This design has been chosen for two reasons. First, it is important that both the participants and the researchers do not know which group they are in (i.e. that they are 'blinded') because that knowledge could affect the measurement of results. This psychological effect can be a particular problem in conditions like carpal tunnel syndrome, where much of the problem caused by the disease is the participant's subjective symptoms. Secondly, it is not yet known whether electrical stimulation will improve participants' outcomes. It is believed that it might improve outcomes, based on one previous study and animal data. However, significant changes (such as the timing of stimulation, and delivering stimulation non-invasively, including participants with non-severe carpal tunnel syndrome) have been made, so the team cannot be sure – hence why the study is running. Everyone in both groups will still get the current gold standard treatment – the operation.

The primary outcome is the change in cold detection threshold (a measure of small sensory nerve fibre function) from pre-surgery to six months post-surgery. This measure was chosen as the primary outcome based on previous work from the group that cold detection is impaired in people with carpal tunnel syndrome, fails to recover completely after surgery and that the degree of recovery predicts overall hand function.

The null hypothesis is that pre-operative electrical stimulation has no effect on cold detection threshold six months after carpal decompression surgery.

Secondary outcomes include:
- other measures of sensation, such as detecting the difference between two pressures
- measures of hand strength
- measures of dexterity
- electrical tests which tell us about the structure of the nerve
- questionnaires which tell us about hand function and symptoms
- MRI (magnetic resonance images) data about the structure of the nerve – these scans are optional and will not be completed in all patients
- Skin biopsies taken from the index finger, which allow us to look directly at nerve fibres as they regrow

Blood tests will be taken that allow an analysis of DNA for the presence of a mutation which may affect the response of nerves to electrical stimulation.
Tissue collection is planned for analysis in future studies covered by separate ethics, including blood samples and tissue from around the nerve which is normally removed and discarded during surgery.

The study plans to recruit 60 patients. The sample size has been determined by the trial statistician based on the primary outcome of change in cold detection threshold at six months. A sample size of 60 provides 80% statistical power assuming 20% missing data. The study is a single centre at an NHS site (a tertiary hand surgery centre). There will be three routes by which participants will be identified and contacted by the study team for recruitment into the study: direct meetings in hand surgery clinics, contact by the study team after clinic visits and identification from hand surgery waiting lists. On average, the centre sees 15 new patients per week with carpal tunnel syndrome and performs 500 carpal tunnel decompression operations per year. This team has successfully recruited CTS patients to previous studies at a rate of more than one per week. As such, they are confident they can reach the 60-patient target within a 72-week recruitment period.

Once enrolled, participants will take part in a total of six in-person study visits to Oxford University Hospitals in addition to their routine surgery visit, with an additional one remote follow-up visit (nine visits total). These visits include one visit for the stimulation and one visit for the operation. Two of these visits are optional for MRI scans of the wrist. During the first visit, electrical testing of the participant's nerve will determine the severity of their carpal tunnel syndrome. Between Visit 1 and 2, participants will be randomised to intervention or control arms, stratified by severity. Given the double blinding, patients are not informed of their random allocation.

Timeframe of visits:
- Visit 1: 2-3 months before surgery for baseline assessment, including first skin biopsy and blood sample. Duration approx 3 hours.
- Visit 2: OPTIONAL MRI scan of the wrist 2-3 months before surgery. Duration approx 1 hour.
- Randomisation occurs (patient blinded and not informed)
- Visit 3: 5-10 days before surgery for intervention - either real or placebo stimulation. Duration approx 1.5 hours
- Visit 4: surgery (normal NHS care)
- Visit 5: 3 months after surgery, including repeat blood sample. Duration approx 2 hours
- Visit 6: OPTIONAL repeat MRI scan of the wrist 3 months after surgery. Duration approx 1 hour
- Visit 7: 6 months after surgery, including repeat skin biopsy and repeat blood sample. Duration approx 2 hours.
- Visit 8 (remote): complete questionnaires only from home 12 months after surgery

In total, participants will complete between ten and twelve hours of study visits in this period (not including surgery), depending on whether they come to the optional MRI visits. Participants will be reimbursed for the visits that are not part of their normal care, up to a total of £200 depending on how many visits they complete.

This design and methodology were originally informed by a James Lind Alliance priority-setting partnership, which identified improving interventions for nerve injury as a top 10 research priority in hand and wrist surgery. The design was further informed by our patient and public partners suffering from nerve injuries of the hand/wrist including carpal tunnel syndrome, by an in-depth focus group and a separate lecture in which the audience opinion was polled. They guided the team on the primary outcome, which was originally planned by an electrophysiologic measure of motor function (motor unit number estimation) by rating sensation as the most important factor in their recovery after overall hand function. A third arm was originally considered in which patients underwent pre-operative stimulation using needles (percutaneous) but this idea was dropped due to strong patient opposition to percutaneous stimulation. The study was also guided by patients in setting the amounts for reimbursement, timeframe for follow-up and willingness to undergo skin biopsies. The language of the patient-facing materials has also been guided by strong patient preference for 'placebo' over our originally used 'sham'.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
DS7A high voltage constant current stimulator

Primary outcome(s)
Cold detection threshold to a thermode (thermal probe) being placed on the skin measured using perception of ramped thermal stimuli at baseline pre-surgery and 6 months post-surgery

Key secondary outcome(s)
1. MRI parameters of median nerve at the carpal tunnel at baseline and 3 months
2. Median nerve sensory and motor conduction studies including motor unit number estimation (assessed by M-Scan method) and axonal excitability
3. Boston Carpal Tunnel Syndrome questionnaire at 12 months
4. Visual analogue rating of symptoms at 12 months
5. iHand nerve function questionnaire at 12 months
6. painDETECT questionnaire at 12 months
7. Neuropathic Pain symptom Inventory at 12 months
8. Depression Anxiety Positive Outlook Scale at 12 months
9. Short-form pain Anxiety Symptoms Scale at 12 months
10. Insomnia Severity Index at 12 months
11. EQ-5D-5L at 12 months
12. Global Rating of Change questionnaire at 12 months
13. Quantitative sensory testing (German Research Network for Neuropathic Pain short form protocol) at baseline and 6 months
14. Histological parameters of median nerve innervated skin biopsy at baseline and 6 months

Completion date
01/08/2026

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study.
2. Male or female, aged 18 years old and over
3. Diagnosed with carpal tunnel syndrome based on clinical examination by a hand surgeon
4. The patient has already determined they wish to proceed with carpal tunnel decompression surgery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
80 Years

Sex

All

Total final enrolment
60

Key exclusion criteria
The participant may not enter the study if ANY of the following apply:
1. Previous major hand, wrist surgery or forearm on the side affected by CTS, defined as previous carpal tunnel release, previous nerve repair, implantation of metalwork
2. Post-traumatic CTS
3. Previous electrical stimulation treatment of any kind, including implanted electrical stimulation devices such as cardiac pacemakers
4. Current pregnancy or CTS which developed during a previous pregnancy
5. Any peripheral neuropathy other than CTS
6. Another medical condition affecting the upper limb and neck (e.g., rheumatoid arthritis, cervical radiculopathy)
7. Diabetes mellitus
8. Hypothyroidism
9. Severe anxiety or depression
10. Conditions affecting pain perception (e.g. fibromyalgia)
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 Study, or may influence the result of the study, or the patient's ability to participate in the study.
12. Evidence of motor conduction block across the carpal tunnel on neurophysiological testing
13. Patients with insufficient command of English to obtain consent from or to complete the study questionnaires.
14. Patients with insufficient mental capacity to obtain consent from or to complete the study questionnaires
15. Patients who in the opinion of the consultant in charge of their care, or the chief investigator, are unsuitable for participation in the study.

Date of first enrolment
01/04/2024

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington

Oxford
England
OX3 9DU

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
British Society for Surgery of the Hand

Alternative Name(s)
The British Society for Surgery of the Hand, BSSH

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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 Max Stewart, mdiv1708@ox.ac.uk

IPD sharing plan summary
Available on request