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# An investigation of the effect of high frequency wave treatment of the spinal nerves on chemicals released into the spinal fluid and bloodstream, and the effect on patient outcomes

| Submission date | Recruitment status | [X] Prospectively registered |
| --- | --- | --- |
| 06/11/2019 | Suspended | [ ] Protocol |
| Registration date | Overall study status | [ ] Statistical analysis plan |
| 01/01/2020 | Completed | [ ] Results |
| Last Edited | Condition category | [ ] Individual participant data |
| 07/12/2020 | Nervous System Diseases | [ ] Record updated in last year |

## Plain English summary of protocol

Background and study aims
Radicular pain (RP) is the most common cause of nerve-related pain in the lower back and legs. It may become a chronic pain (lasting more than 3 months) in 30% of cases. The most frequent cause of radicular pain is disc herniation in patients less than 50 years old, and degenerative spinal disease in the over 50's.

Significant pain relief may be achieved with an injection of a local anaesthetic around the nerves where they exit the spinal column (dorsal root ganglion [DRG]). Additionally, PRF therapy plays a crucial role in the treatment of RP. Studies also report a 100% safety record with PRF with no adverse neurological outcomes.

The aim is to investigate the cellular components (of both blood and spinal fluid) of patients with lower back and leg pain. We will compare the blood and spinal fluid samples both before and after a pain treatment called pulsed radiofrequency

Who can participate?
Patients aged between 18-60 years with chronic low back and leg pain in a definite nerve distribution and a bulging disc present on an MRI scan (which corresponds to the distribution of pain)

What does the study involve?
After consenting, a sample of cerebrospinal fluid (CSF) and a peripheral blood sample will be taken. A PRF procedure will be performed (or simply local anaesthetic if in control group) At standard points post treatment, the patients will be re-assessed

What are the possible benefits and risks of participating?
Inclusion in this study offers no benefits other than to progress the understanding of cause of chronic nerve pain and help us to decide whether we should give all patients PRF treatment or not.
There is a risk of infection, bleeding, nerve damage and headache (1 in 200) related to pain procedure and spinal fluid sampling

Where is the study run from?
Hermitage Medical Clinic, Ireland

When is the study starting and how long is it expected to run for?
January 2020 to December 2020

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Deborah Galvin
deborahgalvin@yahoo.ie

# Contact information

### Type(s)
Scientific

### Contact name
Dr Deborah Galvin

### ORCID ID
https://orcid.org/0000-0002-3506-195X

### Contact details
Trinity Translational Medicine Institute
Trinity Centre for Health Sciences Trinity College Dublin
St James's Hospital
Dublin
Ireland
8
+353 1 896 3268
deborahgalvin@yahoo.ie

# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number

Nil known

# Study information

### Scientific Title
An investigation of the effect of Pulsed Radiofrequency treatment of the Dorsal Root Ganglion on cerebrospinal fluid and peripheral venous blood cellular, proteomic and neuropeptide concentrations with clinical outcome correlation in patients with chronic lumbosacral radicular pain

### Study objectives
We aim to:
1. Identify and quantify changes in the number of neuroimmune cells (CD4+ T cell, CD8+ T cell) and natural killer cells in cerebrospinal fluid and peripheral venous blood samples before and after pulsed radiofrequency therapy in patients with radicular pain
2. Identify changes in neuropeptides and cytokines implicated in neuropathic pain conditions following PRF (BDNF, Substance P, NGF, MCP-1, VEGF, IFN-gamma, IL-1, IL-6, TNF, PDL-1)
3. Characterise the proteome in CSF and VB in patients with RP and the effect of PRF therapy on the proteome
4. Quantify the clinical effect of PRF

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 07/10/2019, Hermitage Medical Clinic Ethics Committee (Old Lucan Road, Dublin, D20 W722, Ireland; +353 1 6459000; ethics@hermitageclinic.ie), ref: none provided

### Study design
Single-center randomized triple-blinded controlled trial

### Primary study design
Interventional

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Chronic, radicular, lumbosacral pain

### Interventions
Patients will be randomised to receive a single session of pulsed radiofrequency therapy (PRF) or a sham procedure.

PRF is a treatment for chronic pain which occurs in the path of a particular nerve(s). A radiofrequency probe with an active tip is placed under fluoroscopic guidance. A small amount of radio-opaque dye is used to identify the nerve root to the epidural space (dorsal root ganglion, DRG).When probe appears in a satisfactory position, sensory stimulation (50 Hz) is sought at an output of less than 0.4 Volts. The probe is manipulated until the patient reports paraesthesia in a distribution concordant with the usual painful distribution. If the paraesthesia

is not elicited in the correct dermatome, another probe will be placed at a neighbouring DRG to map the paraesthesia to the usual pain distribution. Once this is achieved, motor stimulation (2 Hz) at greater than 1.5 times the sensory stimulation is checked. Impedence less than 450 Ohms is required. One ml of lidocaine 1% is applied to the DRG.

The treatment group (LA + PRF) receive one pulsed radiofrequency treatment to the DRG - at less than 420C for 120 seconds with pulses (20 milliseconds at 500,000 Hz) at 2 Hz and a voltage output of 45 Volts.

The patients in the control group (LA) receives 120 seconds free of stimulation.

Follow-up:
Assessments will be made at the following time points:
- Immediately before the procedure (T0)
- 1 hour after the procedure (Global Perceived Effect and Numerical Rating Scale only) (T1)
- 1 month post procedure (T2)
- 3 months post procedure (T3)
- 6 months post procedure (T4)

Randomisation process: Randomisation will be performed in Trinity Translational Medicine Institute. They will use a computerised, random number generator and use block allocations (block sizes of 2 and 4). Patients will be randomised and the RF machine operator (theatre nurse) will be given a sealed envelope to open with the treatment direction when the RF probe is sited. The machine operator will return the form with patient ID and treatment details in a sealed envelope. If the DRG block procedure fails, regardless of whether the patient receives PRF or not, details of the failed block will be included on the randomisation sheet and the patient will be excluded from the study, and another patient will be re-allocated to this group.

## Intervention Type
Procedure/Surgery

## Primary outcome(s)
The concentration of CD4+ T cells measured in the CSF at 3 months (T3) post PRF

## Key secondary outcome(s))
Measured using cerebrospinal fluid and peripheral venous blood samples:
1. NK cell and CD8+ T cell numbers at baseline and T3
2. CD4+/CD8+ ratio at baseline and T3
3. CSF neuropeptide and cytokine concentrations at baseline and T3

Secondary outcomes (clinical):
4. Improvement in symptoms (on the Global Perceived Effect (GPE) - Likert Scale) at baseline and T3
5. Pain score (Numerical Rating Scale [NRS]) at baseline and T3
6. Global Perceived Effect (GPE) on Likert Scale and NRS at one hour (T1), one month (T2), and 6 months (T4) post PRF.
7. Quality of Life measured using the RAND-36 at T2, T3 and T4
8. Functional ability measured using the Oswestry Disability Index at T2, T3 and T4
9. Medication usage measured using the Medication Quantification Scale III at T2, T3 and T4
10. Adverse events at T1, T2, T3 and T4
11. Further interventions required at T2, T3 and T4

### Completion date
31/12/2021

# Eligibility

### Key inclusion criteria
1. Age range 18-60 years
2. Unilateral monosegmental radicular pain in the lumbosacral nerve roots
3. Symptoms consistent with MRI findings of a contained herniated disc
4. Chronic pain lasting more than 3 months
5. Failed conservative medical management for over one month (medication and physical therapy)
6. Radicular pain is the primary complaint with minimal axial pain
7. NRS of > 3 (on 11-point NRS)

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Upper age limit
60 years

### Sex
All

### Key exclusion criteria
1. Patient refusal
2. Atypical or bilateral radicular pain patterns
3. Axial pain
4. Cognitive impairment or language barriers that could impair the patients understanding and reporting of outcomes
5. Malignancy
6. Vertebral fractures
7. Multiple sclerosis
8. Connective tissue diseases
9. Infection
10. Pregnancy or breast-feeding
11. Prior Spinal surgery
12. Lumbar spine interventions in the last 6 months (epidural injections or PRF)
13. Coagulation disorder or anti-coagulant treatment
14. Psychiatric disorder
15. Allergy to local anesthetics or contrast medium

16. Dependent Personnel such as staff members, students or NCHDs
17. Pre-operative NSAID, corticosteroid, methotrexate, monoclonal antibody therapy or opioid therapy
18. Patients will be excluded from the study if appropriate nerve stimulation during the PRF procedure or pain relief (more than 50%) post DRG block are not achieved

### Date of first enrolment
22/01/2020

### Date of final enrolment
30/06/2021

## Locations

### Countries of recruitment
Ireland

### Study participating centre
**Hermitage Medical Clinic**
Old Lucan Road
Dublin
Ireland
D20 W722

## Sponsor information

### Organisation
Trinity Translational Medicine Institute

### ROR
https://ror.org/02tyrky19

## Funder(s)

### Funder type
Other

### Funder Name
Investigator initiated and funded

# Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. Only the three authors will have access to the data. Once journal publication has been achieved the data will be irreversibly deleted. Patients will be identified by code. Data will be stored for 5 years.

## IPD sharing plan summary

Stored in repository

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |