South Tees Hospitals NHS
NHS Foundation Trust

Department of Pain Management
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PARTICIPANT INFORMATION SHEET FOR PARTICIPANTS

Sponsor: Guy's and St Thomas NHS Foundation Trust
Protocol number: Modulate-LBP v1.3 15th July 2019
Ethics Committee reference number: 18/LO/1031

Investigator: Professor Eldabe
IRAS ID: 232729

Study title:

Multicentre, Double Blind, Randomised Placebo-Controlled Trial of 10kHz High-Frequency Spinal Cord Stimulation for Chronic Neuropathic Low Back Pain

Short Title

MODULATE-LBP

Sponsor:

Guy's and St Thomas NHS Foundation Trust

Protocol Number:

Modulate-LBP v1.3 15th July 2019

ClinicalTrials.gov Identifier:

NCTO3470766

Principal Investigator:

Professor Sam Eldabe

Study Site:

South Tees Hospital

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Invitation and Background

We would like to invite you to participate in a research study called Modulate-LBP. You have been invited as you have a history of chronic pain in your lower back. Your doctor has identified you may be a suitable candidate to receive a medical device called a SENZA spinal cord stimulation system, which may help to relieve your pain. If you do not wish to take part in the research you would still be eligible for this device through your normal care.

This information sheet gives you important information about this study to help you decide if you want to participate. It describes the purpose of this study, the study procedures and the possible risks and benefits of participating.

Before you decide whether to take part, it is important that you understand why the research is being done and what it will involve. Please take the time to read the following information carefully. You should talk to the study doctor and study staff about this study and ask any questions you have. You can also discuss this study with other people such as your family or your General Practitioner (GP). If you decide to participate in this study, you will be asked to sign and date a consent form. You will be provided with a copy of the signed consent form.

After you have signed the consent form, the study doctor and his/her study staff will do some assessments to see if you meet the study requirements

You will still be free to withdraw from the study at any time without giving a reason. A decision not to take part, or a decision to withdraw at a later date, will not affect the standard of care that you receive. If you leave the study, unless you object, we will still keep the records relating to the treatment given to you.

Why is this study being done?

The main purpose of this study is to see how well the SENZA spinal cord system eases lower back pain in participants who have not had previous back surgery. We will achieve this by comparing participants who receive active programming with participants who receive inactive programming (placebo).
Spinal cord stimulation systems reduce pain by delivering small electrical fields to the spinal cord. These electrical fields mask areas of pain by changing the pain messages your body sends to your brain and can significantly reduce pain. Participants who receive active programming will receive these small electrical fields to cover the pain. Whereas participants who receive inactive programming will not receive these small electrical fields.

This device requires a minor surgical procedure under x-ray control in which a lead is precisely placed within an area at the back of the spine. The lead is then connected under the skin to a battery device which is surgically sited in the buttock. The battery powers the electrical stimulation of the lead in the spine, once the system is set-up, it can be controlled by using a handheld controller.

How many people will take part in this study and for how long?

We will be recruiting 96 participants and each participant will take part in the study for up to 6 months. The study will be held at 2 centres in England.

What are the chances I will get the active treatment?

Sometimes we don't know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are then compared to see if there are any differences. The two treatment groups in this study are:

- Active Programming
- Inactive Programming (placebo)

Whether you receive Active Programming or Inactive Programming is decided randomly, like flipping a coin. Randomisation is a method based on chance which will be used to determine if you will receive either the study treatment or placebo. You will have a 50% chance of receiving either the Active or Inactive Programming for the 6 month study duration, after this ALL patients will be offered Active Programming.

Will I know which study treatment I am receiving?

This trial is a double blind trial which means that neither you nor the study doctor or study staff will know which treatment you are receiving. In an emergency, the study doctor and study staff are able to find out what programming you were allocated to.

What If I am receiving Inactive Programming during the study?

Study participants assigned to the Inactive Programming group may be able move over to Active Programming after the 6 month follow-up visit. As it is not known how effective the active programming is until after the study is complete there would be no benefit from switching over until the results of study are known.

What would taking part involve?

While participating in this study, you must return for scheduled visits. Please let the site study staff know if you will be unable to do this. A total of 7 visits are planned in this study, but your study doctor may ask you return to the clinic for additional visits. Your participation in the study will last approximately 6 months.

<u>Screening visit</u>

If you decide to join the study, your doctor will ask you to sign an informed consent form; you will be given a copy of this information sheet and your signed informed consent form to keep. A copy will also be placed in your medical notes at the hospital. If you consent for your GP to be informed we will send a letter to the practice.

You are considered enrolled in the study when you have voluntarily signed the consent form.

A suitably qualified nurse will ask you questions about your medical history, pain medications, and if you are a women of childbearing age you may be asked to do a pregnancy test as you cannot be in the study if you are pregnant or planning to have a baby in the next 12 months. This is to protect an unborn baby against any possible unknown effects.

You will be provided with a diary to record your pain score each day for 7 days. You will be asked to bring the diary with you to your next visit.

If you have not had a recent MRI and X-ray your clinician will book for you to have one prior to your next visit. This will consist of a separate appointment with the radiology department. You will receive further information in regards to your MRI/X-ray by the department.
Your name and any information that enables the study staff to identify you will be separated from the information you have provided. This confidentiality may only be broken if required by law or for your own health and safety.

Baseline visit
You will be asked to bring your pain diary to this visit.
During this visit, you will be asked to complete further questionnaires about your pain. Study staff will review your eligibility and determine if you meet study requirements.
If eligible, you will be reviewed by the study doctor and provided with further information regarding your upcoming surgery.

As part of the baseline measurements you may be asked to participate in filming of the distance that you can walk and climb stairs within a specific time. This will also be done at 6 months so a comparison can be made to determine the effect of spinal cord stimulation on mobility. We have a separate consent for this filming as anonymity cannot be guaranteed as your face and body cannot be hidden.

Device full implant
In standard clinical practice most individuals deemed suitable to receive the SENZA spinal cord stimulator undergo a trial period. This temporary trial period involves an initial surgical procedure in which the stimulator will be partially implanted and tested for up to two weeks, after which patients can determine whether it works for them, and choose to either have the stimulator removed, or undergo a second procedure to completely implant the device.

In this study all suitable subjects will receive the whole implant without the temporary trial phase. This is due to our previous study showing a 95% success rate from Trial to Implant. Therefore we deemed the trial period to be unnecessary in this patient population. This means that you will only undergo one surgical procedure as opposed to two, minimising surgical and anaesthetic risk.

The complete implant is done as a minor surgical procedure under x-ray control in a theatre environment. You may be given medication to help you relax. A small cut will be made on your back to precisely place one small insulated lead within an area at the back of the spine.

About a 2 inch cut will be made under your skin forming a "pocket" where the battery device along with a second lead, will be implanted. This pocket is usually made in the buttock area.

The procedure can take between one and two hours.

After the implant, you can expect to feel some pain where the cuts in the skin were made and where the device was placed. This pain is normal. The study doctor may give you some medications to treat your surgical pain. You will also be given antibiotics to help prevent infections. You may or may not be able to feel parts of the device underneath your skin. The implanter will try to place the device where it is easy to reach for recharging, less visible and most comfortable for you. Depending on your body size, the device may be seen as a small bulge under your skin. This will be the same regardless of your participation in the study.

After surgery, your device will be switched off and will remain off for approximately 2-4 weeks to allow time for your wounds to fully heal. This is normal practice.

Randomisation & Device Activation

Once your surgery wounds are fully healed, you will be asked to return to the hospital to have your device switched on. You will be provided instructions on how to charge the battery in your device. You will be shown how to turn your device ON and OFF by using your "patient programmer", like a television remote control.

On this visit you will also be randomly assigned to either Active Programming or Inactive Programming. Your technician will be one of the study nurses who programs your device. The technician will not reveal the group assigned to you, your doctor, or any of the study team. This is to ensure your perception of pain is not affected by the expectation of receiving Active or Inactive programming.

1, 3 and 6 Month Follow up visit

We will see you in clinic at 1, 3, and 6 months. At these visits you will be asked questions about your stimulation therapy, pain, and other questionnaires. Anonymised data from your device will be saved. You will be provided with a diary at each visit to record your pain scores for 1 week before returning for your next visit. You will receive a reminder via text message of when you should begin completing the diary. You should bring your completed diary with you when you next come in.

At the 6 Month Follow up visit you will have the opportunity to continue with your current treatment if you are responding well. If you are not benefiting from the treatment you are on after 6 months, you will have the opportunity to switch treatment or have your device reprogrammed.

Unscheduled visit

It is possible that your device may need to be reviewed or additional treatment may need to be provided to you while you are in the study. If your doctor thinks it is necessary, he will discuss this with you and perform additional tests or investigations as agreed.

What do I have to do?

If you participate in this study, we ask you to assist us with the following. We ask you to be truthful regarding your health, medication use, and complete the study questionnaires to the best of your ability. If other care providers see you, you should tell them that you are in this research study. We also ask you to report any admission to hospital, visits to A&E or other medical visits, symptoms, sickness, injuries or complaints to the study doctor or study nurse as soon as possible. If you are a woman of childbearing age, you must agree to use a medically acceptable method of birth control.

You need to complete entries into a 7 day paper diary over the course of the study and keep your device charged. You need to recharge your device regularly to avoid over-discharge of the battery (complete draining of the battery). We expect you to return to the study doctor's clinic for each study visit within the specified timeframes. If you cannot attend a visit, please call the study nurse on the number provided to reschedule as soon as possible.

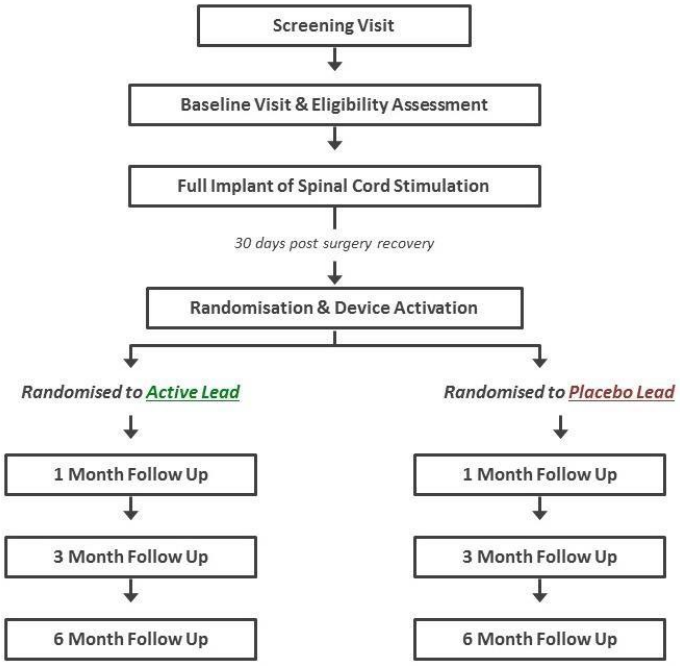

Figure 1. Study Flow

What are the alternative treatments?

There are also other treatments available to you, your doctor will discuss other treatments that may benefit you. You do not have to be in this study to be treated for back pain.

What are the possible benefits of taking part?

Your pain from your existing condition may improve while you are in this study. The potential benefits you may receive include the following:

- Reduced pain
- Reduced pain medication
- Improved quality of life
- Improved quality of sleep
- Improved function
- Ability to return to work

The results of this study may help people with similar types of pain in the future.

What are the possible disadvantages and risks of taking part?

There are risks with any operation but most of the problems that can happen with spinal cord stimulators are minor. There are a few problems that you should know about such as:

Possible Side Effects	How many people it affects
There is a possibility of your current pain condition not improving during the study.	30 in every 100
Failure of system components such as premature battery depletion. This may result in changes in sensation, need to turn off the device or possible replacement of the device component.	10 in every 100
You may experience pain or tenderness in the area where the leads were inserted into your body or the area where the pulse generator (IPG) was implanted	10 in every 100
You may develop an infection and most of these are not dangerous. Your doctor might have to remove the system to prevent the spread of infection even if the system was helping your pain	6 in every 100
The electrode in your spine may move or not work and you may need further surgery to correct	5 in every 100
Possibility that the system will need to be revised (removed, replaced, or repositioned). Possible reasons for revision/removal may include infection, malfunction, migration of the system components, or other reasons. During the replacement/revision/removal procedure, there might be a "build-up" of scar tissue (related to the original surgery) that may make removal or replacement of the leads unsafe and the leads would be abandoned.	4 in every 100
You may experience some discomfort or pain during stimulation. If the pain is excessive you may be asked to leave the study and have spinal cord stimulator removed	3 in every 100
The use of anaesthesia in surgery comes with risk of adverse reaction to aesthetic agents. Such reaction include dry/sore throat, nausea vomiting, sore muscles, sore jaw and short term memory loss or confusion. The vast majority of subjects recover from these side effects in a day or so.	1 in every 100
Bleeding, which may lead to bruising and in rare cases may require further surgery	1 in every 300
Severe headache due to leakage of cerebrospinal fluid, which may require treatment with a spinal injection if it does not improve	1 in every 300

These are the published data of risks from spinal cord stimulator implant surgery from 2015. If you do decide to take part in the study, you must report any problems you have to your study nurse or doctor. Additionally, the treatment is reversible and the device may be turned off at any time should you experience any discomfort. There is also a contact number given at the end of this information sheet for you to phone if you become worried at any time.

Possible Serious Side Effects

There are some possible serious side effects to receiving spinal cord stimulator. These are very rare and are the same for any general surgery.

Possible Serious Side Effects	How many people it affects
Hematoma (a collection of blood outside of a blood vessel, it occurs because the wall of a blood vessel, artery, vein, or capillary, has been damaged and blood has leaked into the tissue) resulting in localised paralysis.	1 in every 1000
There is a risk of unexpected and unusual reactions to the anaesthesia that can lead to heart problems such as a heart attacks or lung problems such as respiratory failure.	1 in every 1000
As with any operation in the spine, there is a very small risk of nerve damage, trauma to the spine and localised paralysis. This is something we look out for in the first few hours after your operation	1 in every 3000
All procedures involving anaesthesia carry the risk of death.	1 in every 10,000

Other Possible Disadvantages/Side Effects

- Subjects on blood thinners (e.g. warfarin/aspirin) may have greater risk for postoperative complications. It is important that you mention if you are on blood thinners your doctor will discuss options with you to reduce these risks.
- Possibility of receiving no active treatment for 6 months if allocated to inactive programme
- Insertion of second lead near buttock potentially carries the following risk, the frequency is the same as above:
  - Localised infection
  - Bleeding
  - Lead migration
  - Rarely skin wear

- **For Women:**

Women who are pregnant or nursing a child cannot take part in this study because we do not know if the stimulation would affect the baby and you will be exposed to X-rays during the implantation procedure. If you get pregnant during the study, you must tell your study doctor immediately and switch off your SCS device. If you are a woman who might become pregnant you must agree to use a 'dual'/two effective methods of contraception during the trial e.g.

-Oral contraceptive + condom
-Intra-uterine device (IUD) + condom
-Diaphragm with spermicide + condom

There may be other risks or discomforts to you (or to an embryo, unborn child or nursing infant if you become pregnant) that are not known at this time. If important information is learned during the course of this research study, your doctor will discuss this important new information that is learned during the course of this study that may affect your condition or willingness to continue to take part in this research study.

Ionising radiation

If you take part in this study you will have X-ray/Fluoroscopy as part of the initial assessment for the study and during the spinal cord stimulator implant procedure. Some of which will be extra to those that you would have received if you did not take part. These procedures use ionising radiation to form images of your body and provide your 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 life. Taking part in this study will add only a very small chance of this happening to you.

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions further contact details can be found below. Should you have any concerns regarding your overall health at any point, such as worsening of condition or if you feel distressed or anxious at any point during the research study, please discuss this with your study team who will assure you receive the correct specialised care.

If you remain unhappy and wish to complain formally, you can do this through:

The PALS team and they can be contacted on freephone: 0800 0282451, or on 01642 854807/01642 282657 (internal extension numbers 54807 or 52657 JCUH)

Post:
Patient advice and liaison service (PALS)
The James Cook University Hospital
Marton Road
Middlesbrough
TS4 3BW

Email: stees.pals@nhs.net

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against Guy's and St Thomas NHS foundation trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

What if relevant new information becomes available?

Sometimes during the course of a study, new information becomes available. If this happens, we will tell you about it and discuss with you whether you want to or should continue in the study. If you decide to withdraw, we will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

On receiving new information, we might consider it to be in your best interests to withdraw you from the study. If so, we will explain the reasons and arrange for your care to continue.
If the study is stopped for any other reason, including by the sponsor, you will be told why and your continuing care will be arranged.

Will you receive payment for taking part in this research study?
You will not receive any payment for your participation in this study; however, reasonable travel expenses for study visits outside of your routine care will be reimbursed to you. In this study there is only a single study visit outside routine care in which you will be able to claim reimbursement for travel expenses. Please speak to your study staff for further information.

Informing your General Practitioner (GP)
With your permission, you're GP, and other doctors who may be treating you, will be notified that you are taking part in this study. Should you or your GP have questions or concerns about anything you have read you should discuss this with the study nurse or doctor.

Will my part in this study be kept confidential?
If you consent to take part in this study, the information obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper at your treating hospital under the provisions of the 1998 Data Protection Act. Your name will not be passed to anyone else outside the research team or the sponsor, who is not involved in the trial. You will be allocated a trial number, which will be used as a code to identify you on all trial forms.

X-ray/MRI imagining may be published and shared with collaborators to assess if there are any changes in the spinal cord of individuals with back pain. The images will be fully anonymised and will not contain any identifiable information

Your name will only appear on your consent form, which will remain at your hospital. All other records will have your name removed and will only feature a special code related to you and your year of birth.

The data collected as part of the study will be uploaded on an electronic system provided by **Exeter Clinical Trials Unit** for analysis. This data will not contain any identifiable information, your allocated trial number will be used to link the data to you.

Your records will be available to people authorised to work on the trial but may also need to be made available to people authorised by the Study Sponsor, which is the organisation responsible for ensuring that the study is carried out correctly.

The information collected about you may also be shown to authorised people from the UK Regulatory Authority and NHS Ethics Committee; this is to make sure that the study is carried out to the highest possible scientific standards. All will have a duty of confidentiality to you as a research participant. Study information collected about you will be given to the sponsor. The study information, but not your personal information (name, address etc.), may be looked at and/or copied for research or regulatory purposes by the study sponsor and other regulatory authorities.

If you withdraw consent from further study treatment, unless you object, your data will remain on file and will be included in the final study analysis.

In line with Good Clinical Practice guidelines, at the end of the study, your data will be securely archived for a minimum of 5 years. Arrangements for confidential destruction will then be made.

What will happen to the results of this study?

The results of the study will be available after it finishes and will usually be published in medical journals or be presented at scientific conferences and at meetings with patient representatives. The data will be anonymous and none of the participants involved in the trial will be identified in any reports or publications.

Once results of the study are published your study doctor will pass the information to you via email or letter, depending on your preference.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search the Website at any time.

Who is organising and funding this study?

Funding for this study was obtained through NIHR Research for Patient Benefit Competition 31.

Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, well-being and dignity. This study has been reviewed by:
London-Camberwell St Giles Research Ethics Committee

Contacts for further information

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the procedure(s) involved. If you wish to read the background information on which this study is based, please ask your study nurse or doctor. If you require any further information or have any concerns while taking part in the study please contact one of the following people:

Your Doctor: Professor Sam Eldabe 01642 282417

Your Study Nurses: Morag Brookes 01642 282820 or Sara Griffiths 01642 835971