Departments of Anatomy and Neurosurgery
Otago School of Medical Sciences / Dunedin School of Medicine
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Principal Investigators:
Professor John Reynolds, Dept of Anatomy
Professor Dirk De Ridder, Neurosurgeon and Professor of Neurosurgery
Professor Leigh Hale, Dean of School of Physiotherapy,
Dr Nick Cutfield, Neurologist, Dept of Medicine

PARTICIPANT INFORMATION SHEET

External (brain) Stimulators To Augment stroke Rehabilitation Therapy (eSTART)

Locality:	**Dunedin**	Ethics committee ref.:	**19/STH/94**
Lead investigator:	**Prof John Reynolds**	Contact phone number:	**Dept. of Anatomy: 03 479 5781**

Thank you for showing an interest in this project. Please read this information sheet carefully before deciding whether or not it is appropriate for you to take part. Your participation is entirely voluntary. If you decide not to take part, you don't have to give a reason, and it will not affect any future care or treatment. If you do agree to take part in the study, you are free to withdraw at any time without having to give a reason and this will in no way affect any future health care.

This Patient Information Sheet explains what the study will involve and will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as your legal representative, family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 10 pages long, including the Consent Form. Please make sure you have read the rest of this information sheet carefully and understood all the pages.

What is the Aim of the Project?

The aim of this study is to improve movement recovery in the arm and hand affected by your stroke by stimulating a part of the brain called the 'motor cortex' using electrical current. The current will be administered externally to your scalp by a brain stimulator and will be applied on the side of the brain opposite to that affected by your stroke.

A stroke is caused by the interruption of normal blood flow within the brain. This results in death of brain cells normally supplied by those blood vessels. Recovery from a stroke requires nerve cells in adjacent brain areas to take over some of the lost function. However, this is resisted by other parts of the brain that tend to 'turn off' or 'inhibit' this change in function.

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One of the likely offending areas is the motor cortex on the side of the brain opposite to that affected by your stroke. We plan in this study to alter the activity of this area using an external brain stimulator capable of delivering 'bursts' of electrical pulses. When applied in conjunction with a physiotherapy programme, we hope that neurostimulation applied to the motor cortex will lead to greater recovery than can be obtained by physiotherapy alone.

We have studied this idea in models of stroke and found that our approach improves function. We now wish to determine if this approach will be feasible in humans who have arm and hand movement difficulties after stroke. First, we will use a magnetic form of brain stimulation to identify how well participants may respond to this treatment. This is called transcranial magnetic stimulation (TMS). Then we will apply at each physiotherapy session the external electrical stimulator to the scalp in a position thought to be optimal to activate the motor cortex.

We don't intend in the long term that this neurostimulation will replace physiotherapy, which is the standard approach to improve your movement and function after stroke. Instead, we hope to find a method that will maximise and maintain the gains that can be obtained from these therapies. If you are currently receiving any other community rehabilitation, you may still be eligible to participate, but we will discuss this with you during enrolment to ensure that participation in our study does not affect your current therapy.

What will Participants be Asked to Do?

Potential participants will have a visit scheduled at the School of Physiotherapy with a clinically-qualified investigator to determine if you are a suitable candidate for the study. You will be fully informed about the study and given an opportunity to ask questions and time to consider whether you wish to participate. If you agree to participate you will be asked to sign a consent form.

Following consent, you will undergo the following study phases:

1. Baseline assessments
2. Intervention (Rehabilitation with/without stimulation)
3. Post-intervention assessments
4. Home programme for 6 months
5. Follow-up assessments

The flowchart of the study protocol can be found overleaf and the details of each phase follows.

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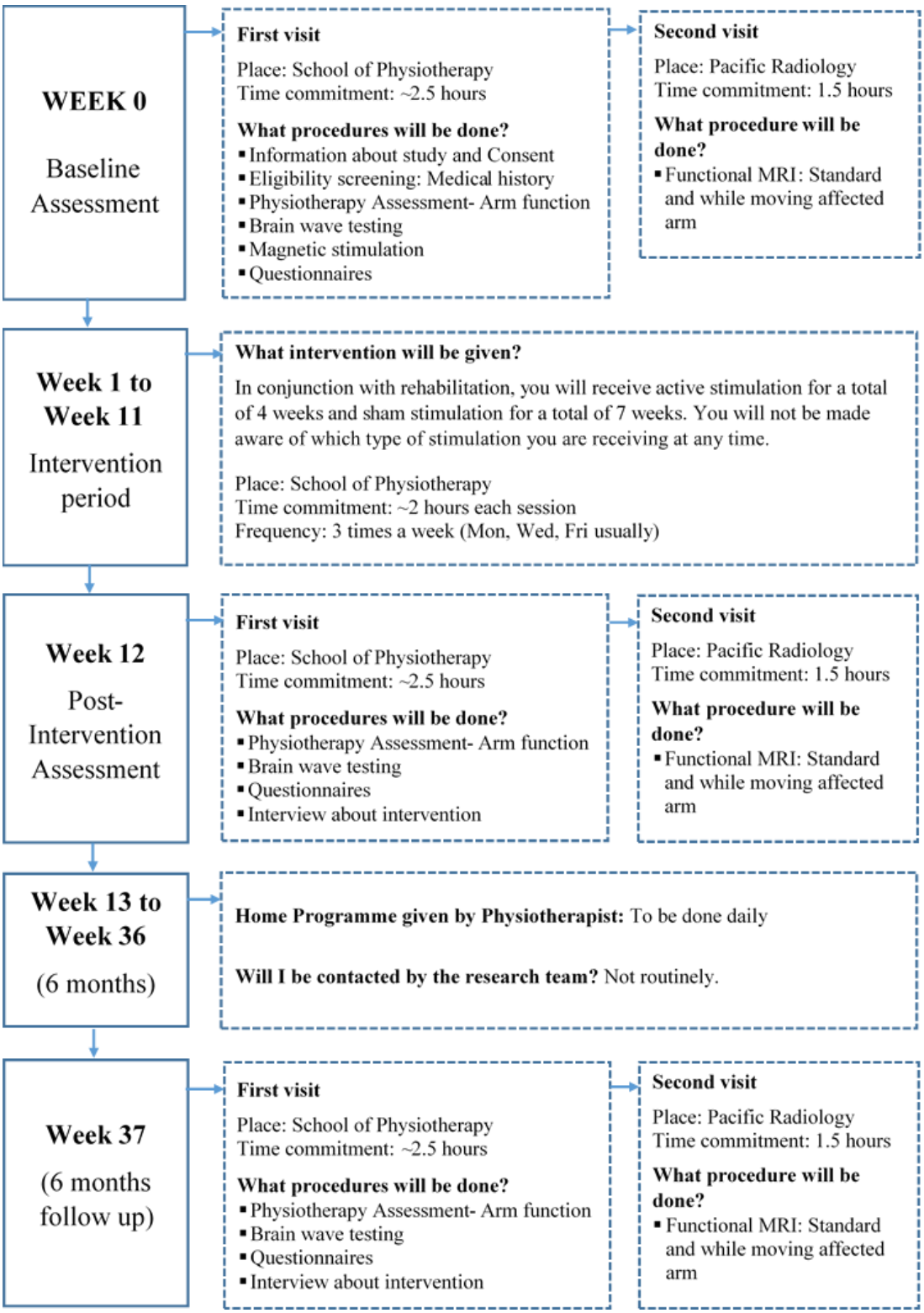
Flowchart of the study protocol



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Baseline assessments (Week 0):

- An examination of the degree of disability you experience from the stroke will be done, and you will be asked about any history of seizures, other medical disorders, and medication usage.
- Brain wave tests (EEG) will be performed during screening, during some of the physiotherapy and stimulation sessions (the 'intervention'), and 6 months after the neurostimulation therapy, to allow us to check for signs of changes in connections between different areas in the brain.
- Pre-intervention magnetic stimulation (TMS) will be performed to determine the strength of the circuits between the motor cortex on the side of your stroke and your affected muscles. This involves placing a special coil on the scalp, which will stimulate the motor cortex with a single magnetic pulse. The size of the pulse will be turned up to a level that might produce a visible muscular twitch. Electrodes will be placed over a number of muscles in your affected arm and hand to enable us to record the effect of the pulse on muscle activity. You will also be asked to wear a cap with stimulation electrodes attached. The wires from the electrodes will be connected to an external stimulator and the parameters of the electrical pulses will be determined in conjunction with the response to the magnetic stimulation (TMS) procedure. This will enable us to set the correct intensity settings ready for activation during the rehabilitation sessions.
- An assessment will be undertaken by a physiotherapist who is one of the investigators in the study. This will measure the baseline level of function in your shoulders, arms, and hands. You will be asked to carry out simple arm movements (e.g. 'brush your hair' or 'pick up an object from the table' etc). Questionnaires will be administered to determine your own assessment of your general wellbeing after stroke and the level of impairment you experience with the affected limb.

If the assessments performed above indicate that you are likely to gain additional benefit from the neurostimulation procedures, you will proceed to have a pre-intervention brain scan (fMRI) to check the position and size of the stroke and to help us determine the brain activity and connections around the stroke area. This will involve you lying still in the scanner for an hour and moving your hands one at a time when asked. If it is considered unlikely to be of additional benefit for you to receive the neurostimulation or physiotherapy rehabilitation procedures, or if you decline either procedure, you will not be eligible to participate in the further stages of the study.

Intervention (Week 1-11): Following baseline assessment, you will immediately begin to attend rehabilitation sessions from the following week at the School of Physiotherapy three times a week (i.e. Monday, Wednesday and Friday usually) for a total of 11 weeks. Each session will be approximately one-two hours and will involve a circuit of exercises individualised around your level of arm and hand abilities. At each session, you will be wearing a cap with the stimulation electrodes attached. Up to 30 minutes prior to beginning the exercises, a trained investigator will set up the parameters of the external stimulator. This will either ensure that the stimulation is switched on throughout the session or the stimulation will remain off. Every participant will receive (i) stimulation with the current switched on

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('active' stimulation) throughout the rehabilitation session for a total of 4 weeks and (ii) stimulation with the current off ('sham' stimulation) throughout the rehabilitation session for a total of 7 weeks. Participants and physiotherapists will not know which period of time the stimulator will be active for (but this can be revealed in the event of an emergency). This is to eliminate a placebo effect of treatment and to enable us to determine whether any improvements you are experiencing in your movements are due to the neurostimulation in conjunction with the rehabilitation or due to the rehabilitation alone. It is very important to attend the rehabilitation sessions, in order to obtain the benefits from the stimulation procedures. You will also be given a home exercise programme to do every day as recommended by the physiotherapist.

The physiotherapy assessment of level of arm and hand function will be repeated at 3, 7 and 12 weeks of the intervention phase and 6 months after completion of the intervention, to monitor the effect of the neurostimulation on your hand and arm movements and level of function.

Post-intervention assessment (Week 12): At the 12-week point, the neurostimulation and rehabilitation sessions will be completed. The physiotherapy assessment, brain scans (fMRI), and the brain wave testing (EEG) will be repeated. You will then be given a home programme to carry out for a further 6 months (Week 13 to Week 36). During this time there will be minimal interaction between the research team and you, except if you have any enquiries.

Follow-up assessment (Week 37): At 6 months post-completion of the intervention, we will schedule appointments for you for a repeat physiotherapy assessment, brain scan, brain wave testing, and to be evaluated using the same questionnaires that you completed at the start of the study. This will determine if the stimulation and rehabilitation has had lasting effects.

Interviews: At the 12-week point and 6-months post-completion of the intervention, you will also be invited to take part in some research to evaluate your experiences with the neurostimulation and rehabilitation study, to help us design similar future studies. This will consist of a series of interviews conducted by the physiotherapy team. These interviews will use an open-ended question technique. You will be able to talk freely. The interviewers will record these interviews by audio-recorders. The recordings will be transcribed word for word. You will have the opportunity to comment on your transcribed interview if you so wish. The open-ended technique of questioning means that the precise nature of the questions that will be asked has not been determined in advance. Consequently, the Human Ethics Committee is aware of the general areas to be explored in the interview but has not reviewed the precise questions to be used. You are reminded of your right to decline to answer any particular question(s) if you wish.

What Type of Participants are we looking for?

- Men and women, aged at least 18 years, who have had a stroke affecting their hand or arm function at least 4 months earlier, which was confirmed by a previous head scan result (either CT or MRI).

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- Participants must have a supportive social network (minimum 1 person) that they will provide contact details for, who will be willing to sign the consent form and to support the participant to attend appointments.

Please make sure that you inform the study staff if <u>any</u> of the following criteria apply to you. This would make you ineligible for participation in this study and could lead to dangerous side effects:

- A history of epileptic seizures
- Presence of a pacemaker or defibrillator
- A reason why you cannot undergo an MRI e.g. metallic implants, severe claustrophobia
- Females who are or intend to become pregnant
- The presence of pain or significant movement restrictions or chronic disease (other than stroke) that would independently cause significant disability or weakness of your affected upper limb.

What Are The Side Effects And Risks?

External electrical stimulation is a safe procedure and will be conducted based on the recommended safety guidelines. The side effects and risks of participation are:

1. Unexpected consequences of the neurostimulation itself, such as the onset of seizures or movement twitches. Stopping the stimulation should stop these side effects.
2. That the stimulation may not improve the movements or function in your stroke-affected limb. It is possible that you may never have any benefit, or, after an initial successful effect, that the benefit wears off.
3. That the stimulation could possibly cause your arm and or hand function to worsen. However, this is highly likely to be only temporary and will reverse after the stimulation procedures are stopped.
4. Other side effects might include mild tingling or itching sensation or transient redness under the stimulation electrodes, fatigue, and headache.

Will I be paid for my participation on this project?

No, you will not be paid to participate in this study. However, we will reimburse any out-of-pocket expenses that you or your support person incur from participating in the assessment appointments e.g. travel expenses to attend appointments at baseline, 3 weeks, 7 weeks, 12 weeks of intervention, and at 6 months post-intervention.

Will there be any costs for my participation on this project?

No. There will be no costs for you regarding this project.

Can Participants Change their Mind and Withdraw from the Project?

You may withdraw from this project at any time and without any disadvantage of any kind. In addition, the study staff may decide to withdraw you from the study if you have any unexpected side effects from the treatment or if they have any other concerns.

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What Information will be Collected and What Use will be Made of it?

We will be collecting and storing information from you regarding your relevant medical history along with information gathered during your physical examination. Prior to intervention, you will have an MRI scan and EEG testing. As outlined above you will have various measures of your ability to move, your level of function and the strength of your movement circuits recorded by way of questionnaires, muscle recordings and physiotherapy assessments. The information from all of these tests will also be stored and analysed. If you decide to participate in this study we will inform your GP and other medical professionals currently involved in your medical care of your decision.

The results of this study will be published in an international scientific journal. The data included in this publication will in no way be linked to any specific person and your identity will not be recorded with the data. If you want access to your personal data later you will need to record the identification number used for your particular tests. You are most welcome to request a copy of the results of the project should you wish. These will be available once all the data is analysed, two years following the commencement of the study, nominally in early 2021.

The data collected will be securely stored in such a way that only those involved in the research program will be able to gain access to it. At the end of the project any personal information will be destroyed immediately except that, as required by the University's research policy, any raw data on which the results of the project depend will be retained in secure storage for ten years, after which it will be destroyed.

Support Person

The researchers believe that it is important for your safe participation in this study that you have a person available to provide support to you during this study. It is important that you identify a suitable person who is willing to provide this role.

The support person:

1. Will be fully informed about the study in the same way that you are.
2. Will be required to sign a consent form indicating that they understand the study and are willing to provide you with support over the 9-month study duration.
3. Should be someone that you are happy to confide in and is aware of your current impairments due to the stroke.
4. Will contact the study team or other suitable medical professional if they have concerns for your health or welfare.

The support person is someone who should be able to assist you to attend study appointments, is willing to advocate for you if necessary, can be a point of contact for the study team if you are not available, and will provide general support for you if necessary.

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ACC statement

In the unlikely event of a physical injury as a result of your participation in this study, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have any questions about ACC please feel free to ask the researcher for more information before you agree to take part in this trial. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

Health and Disability Statement

If you have any queries or concerns about your rights as a participant in this study you may wish to contact a Health and Disability Services Consumer Advocate, telephone: (03) 479 0265 or freephone 0800 37 77 66 or freefax 0800 2787 7678 (0800 2 SUPPORT) or email advocacy@hdc.org.nz. If there is a specific Maori issue/concern please contact Professor John Reynolds at 03 4798781.

What if you have any Questions?

If you have any questions about our project, either now or in the future, please feel free to contact us via:

Dr Divya Adhia **Research Fellow** **Department of Surgical Sciences,** **University of Otago, Dunedin**	Contact phone number: 03 470 9337 Email: divya.adhia@otago.ac.nz or leave a message with the Dept of Anatomy, 03 479 7362.
Prof John Reynolds **Dept. of Anatomy,** **University of Otago, Dunedin**	Contact phone number: 03 479 5781 Email: john.reynolds@otago.ac.nz
Prof Dirk De Ridder **Department of Surgical Sciences,** **University of Otago, Dunedin.**	Contact phone number: 03 470 9337 Email: dirk.deridder@otago.ac.nz

If after hours and/or urgent please contact the above via Dunedin Public Hospital (03 474 0999).

This project has been reviewed and approved by the Southern Health and Disability Ethics Committee (Ref: 19/STH/94).

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CONSENT FORM FOR PARTICIPANTS AND SUPPORT PERSON(S)

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I have read the Participant Information Sheet concerning this project. All my questions have been answered to my satisfaction. I understand that I am free to request further information at any stage.

Interpreters may be available on request. Please make the study staff aware if you would like an interpreter to be available.

1. I have read and I understand the information sheet dated 11/06/19 for volunteers taking part in the study designed to assess the effect of motor cortex neurostimulation on recovery after stroke. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
2. I have had the opportunity to use whānau support or a friend and/or legal representative to help me ask questions and understand the study.
3. I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and this will in no way affect my future health care.
4. I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
5. I understand that the treatment will be stopped if it should appear harmful to me.
6. I understand the compensation provisions for this study.
7. I have had time to consider whether to take part in the study.
8. I know who to contact if I have any side effects from the study.
9. I know who to contact if I have any questions about the treatment used in this study or about the study in general.
10. I wish to receive a copy of the results. Y N
11. If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be used. Y N
12. I agree to my GP or other current provider being informed of my participation in this study. Y N

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I _____ hereby consent to take part in this study.

Participant Signature:	
Date:	

The involvement of a support person is recommended by the researchers.

I _____ hereby consent to supporting the above participant during this study.

Support Person Signature:	
Date:	
Full name of researcher obtaining consent:	
Project role:	
Signature:	
Date:	

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