Patient Information Sheet and Informed Consent

Project: “Transcutaneous Spinal Cord Stimulation (tSCS) to Improve Upper Limb Function in People with MS”
Sponsor: Hospital del Mar Research Institute
Principal Investigator: Pablo Villoslada
Centers: Hospital del Mar / Hospital Clínic / Hospital Sant Pau
Version: 1.1
Date: 14/04/2025

Patient Information Sheet

We are contacting you to inform you about a research study in which you are invited to participate. The study has been approved by the Ethics Committee of Hospital del Mar. Our intention is to provide you with the correct and sufficient information so that you can decide whether or not to participate in this study. Please read this information sheet carefully, and we will clarify any questions you may have. You may also consult with anyone you consider appropriate at any time.

Who is invited to participate?

You are invited to participate in this study because you have been diagnosed with Multiple Sclerosis (MS). Participation in this study is voluntary, and you may choose NOT to participate. If you decide to participate, you may withdraw your consent at any time without this affecting your relationship with your physician or causing any harm to your medical care.

What is the purpose of this study?

In this study you will undergo spinal cord electrical stimulation. Transcutaneous spinal cord stimulation (tSCS) is a non-invasive technique that delivers small electrical impulses through the skin to 'activate' certain parts of the spinal cord. The idea is that, by sending these electrical signals externally (usually through patches placed on the back), communication between the brain and body may be enhanced, especially when there is spinal cord dysfunction such as in MS. This technique is safe, non-invasive, and has shown positive effects in other spinal cord injuries. It is generally not painful, often perceived as tingling or vibration on the skin, although individual perceptions vary. The study is randomized, meaning that allocation to true tSCS or placebo is determined randomly. The placebo will mimic the tSCS procedure but without therapeutic stimulation. The main

objective is to evaluate efficacy using clinical parameters. Participants initially randomized to placebo may later enter an open-label phase to receive active tSCS.

What data will be collected and what procedures will be performed?

Participants with MS will first complete a 6-week run-in period with standard occupational therapy, followed by randomization to 6 weeks of tSCS or sham stimulation, both combined with ongoing therapy. Sessions will take place at the rehabilitation center of Hospital de la Esperanza, in a seated position. Electrodes will be placed on the posterior neck and stimulation sessions will last about 30 minutes, three times per week (preferably Monday, Wednesday, Friday). Sham sessions will use identical equipment without active stimulation. Those initially randomized to placebo will be eligible for open-label tSCS after study completion.

What assessments will be performed?

To assess the functional capacity of the hands and to objectively determine whether there is improvement after treatment, different tests will be used:

- **9-Hole Peg Test**
  The main test is the 9-Hole Peg Test (9HPT), which is a very simple and quick test used to measure hand coordination and dexterity. The person is asked to take small pegs (usually 9) and place them, one by one, into holes in a small board. Then, they must also remove them one by one. The time taken to complete the task is recorded. The test is performed first with one hand, and then with the other. In people without motor difficulties, the test usually takes between 20 and 40 seconds per hand. In people with neurological or coordination problems, it may take a little longer, but it is still a very quick and simple test.
- **Action Research Arm Test**
  Another test that will be performed is the Action Research Arm Test (ARAT), which is a simple but very useful clinical test to evaluate how the arm moves and how functional it is. It is particularly designed for people with spinal cord injuries or other neurological conditions that affect the use of the arm and hand. During the test, the person must perform different tasks with the arm, such as grasping, lifting, releasing, and moving objects of different sizes. These activities are similar to those performed in daily life, such as holding a cup, picking up a small ball with the fingers, or moving a block from one place to another. This allows professionals to directly observe how well the affected arm can be used. The evaluation is organized into four areas: grasp, grip, fine motor coordination, and gross arm movement. Each of the 19 tasks is scored according to whether the person can perform it, how much effort it requires, and whether it is

successfully completed. The ARAT usually takes between 5 and 15 minutes, depending on the patient's mobility.

- **Questionnaires**
  In this clinical trial, three types of questionnaires will be administered to evaluate how participants feel and how they progress during the study:
- **NeuroQOL – Upper Extremity Function:** This test helps us understand how well a person can use their arms and hands to carry out daily activities such as dressing, writing, or lifting objects. It is important to assess improvements in mobility and independence.
- **Modified Fatigue Impact Scale (MFIS):** This questionnaire measures how fatigue affects daily life. It asks about physical, mental, and emotional fatigue experienced during the day, and how it interferes with normal activities such as working, concentrating, or socializing.
- **Global Impression of Change (GIC):** In this test, participants will be asked to indicate whether they feel they have improved, worsened, or remained the same since the beginning of the study. This provides a simple way to capture their personal perception of change.

What are the potential benefits of participating?

Upper limb function will be evaluated during the study. If tSCS is beneficial, you may notice improvements in motor function and daily activities.

What are the possible side effects?

Possible adverse effects include tingling, pressure, or discomfort at the stimulation site. Rare effects include skin lesions, itching, swelling, discoloration, muscle pain, mild burns, dizziness, or changes in blood pressure. These are generally mild and transient. Any adverse events will be covered by the study insurance (HDI Global). You will also be able to contact your MS Unit physician.

Pregnancy warning: pregnant women cannot participate. If you suspect pregnancy, please inform the team before signing.

How is your privacy protected?

Your data will be collected, stored, and used for the purposes of this research and potential publications. Both the sponsor and the investigators are responsible for appropriate data protection (see Annex 1).

Future research use of your data

After the study ends, your data may be important for future MS and neurological research. These studies will require Ethics Committee approval. You may choose whether or not to allow anonymized data use in future studies. Your participation will not be affected by this decision.

Will you receive compensation?

The study treatment and assessments are free of charge. There is no financial compensation for participation. Travel expenses related to therapy visits will be reimbursed.

Can you withdraw?

Participation is voluntary. You may withdraw at any time without explanation and without affecting your care. If you withdraw, previously collected data will not be used.

What happens after the study ends?

If you demonstrate objective clinical improvement and wish to continue, your neurologist may request tSCS treatment through the Neurology Department for outpatient care.

Who to contact?

If you have questions or wish to withdraw, please contact the study team.

Contact:
Dr. Pablo Villoslada Díaz
(pablo.villoslada.diaz@hmar.cat)
Multiple Sclerosis Unit
Hospital del Mar Research Institute
Passeig Marítim de la Barceloneta, 25-29, Barcelona-08003
Tel: 93 248 5033 / 932 483 235

Annex 1: Data Protection

The hospital is responsible for all the data contained in the medical record that can identify you, and the investigators are responsible for the data collected in this study in a coded (pseudonymized) form. The role of the data controller is to ensure that your information is used correctly, in particular by applying the appropriate technical and organizational measures to guarantee that the data are processed in accordance with the applicable regulations. Both the sponsor and the center will ensure that the principles set out in national and European data protection regulations are complied with:

- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 (GDPR) on the protection of natural persons with regard to the processing of personal data and on the free movement of such data.
- Organic Law 3/2018 of 5 December, on the Protection of Personal Data and guarantee of digital rights (LOPDPGDD) and any other implementing regulations.

Confidentiality of your data will be maintained at all times. To protect your privacy, during your participation in the study you will be identified by a code. Only this code will be used to identify your data. The key to the code will be kept in a secure location at the hospital. When your data are processed, only this code will be used. This will also apply to reports and publications arising from the study.

Who can see your data?

Access to your personally identifiable information (non-coded, such as your name or other personal information) will be restricted to the study physician/collaborators and other personnel verifying that the investigators are conducting the study properly and reliably. The following people may access your data:

- Members of the committee overseeing study safety.
- Personnel authorized by the sponsor (study monitors or auditors), when necessary to verify data, study procedures, and compliance with Good Clinical Practice standards; always maintaining confidentiality.
- National and international regulatory authorities, such as the Spanish Agency of Medicines and Medical Devices (AEMPS), foreign health authorities (EMA), and the Research Ethics Committee (CEIM).

Your identity may be disclosed in exceptional cases, such as medical emergencies concerning your health or legal requirements. The processing, communication, and transfer of participants' personal data will comply with the applicable regulations.

Your personal information will only be shared with your authorization and if it is necessary to deliver the study medication to your home. These persons will maintain the confidentiality of your data. We request your permission for this access.

How long will your data be kept?

Your data will be kept by the Sponsor and the investigator at the hospital for at least 25 years after study completion, in accordance with the legal time limits established by clinical trial regulations. The hospital will retain your data for as long as necessary to provide appropriate care (according to medical record regulations).

What rights do I have?

Regarding your data, you have the following rights, which you may exercise with the principal investigator and/or the hospital:

- You may ask at any time what data are being stored (right of access), who is using them and for what purpose; you may request a copy of your personal data for your own use.
- You may request to receive a copy of the personal data you provided in order to transmit them to others (right to portability).
- You may correct your personal data and limit the use of inaccurate data (right to rectification and erasure).

- You may object to the use of your personal data or restrict it (right to object).

Please note that there are some limitations regarding your rights in order to guarantee the validity of the research and to comply with the sponsor's legal obligations and the requirements of medicine authorization. If you decide to withdraw from the trial or revoke your consent for data processing, data already collected up to that point cannot be deleted. Be aware that withdrawal of consent for data processing may result in termination of your participation in the trial.

To protect your rights, we will use the minimum amount of information possible. You are also informed of your right to lodge a complaint with the Data Protection Agency regarding any action by the Sponsor or the Hospital that you believe infringes your data protection rights.

Who can I contact?

You may contact the Data Protection Officer (DPO) of your center, or the DPO of the sponsor:

Contact details of the principal investigator or the DPO of the Center/Institution: Hospital del Mar
DPO contact details: protecciodedades@parcdesalutmar.cat

Can you withdraw your consent regarding the use of your data?

You may withdraw your consent regarding the use of your data at any time. Please inform your study physician. This applies to the use of your data in this study and in future research. Please note: if you withdraw your consent after data have already been collected, the investigators may still use this information.

Informed Consent Form (1/2)

Project Title: “Transcutaneous Spinal Cord Stimulation (tSCS) to Improve Upper Limb Function in People with MS”

Sponsor: Hospital del Mar Research Institute
Principal Investigator: Pablo Villoslada
Study Code: MS03

Center: .....
Initials: .....

I (participant name), ...

I have read and understood the information provided.
I have had the opportunity to ask questions.
I have received sufficient information about the study.
I have spoken with (investigator name): .....
I understand that participation is voluntary.
I understand that I am free to withdraw at any time without explanation, without affecting my medical care or rights.
I understand I will not receive any financial benefit from participating.
I freely consent to participate and authorize the use of my data under the conditions described.

Yes ◯
No ◯

I authorize the anonymized use of my data in future scientific research, ensuring confidentiality.

Yes ◯
No ◯

Patient signature	Investigator signature
Name:	Name:
Date:	Date:

This document will be signed in duplicate: one copy for the investigator and one for the patient

Informed Consent Form (2/2)

Project Title: “Transcutaneous Spinal Cord Stimulation (tSCS) to Improve Upper Limb Function in People with MS”

Sponsor: Hospital del Mar Research Institute
Principal Investigator: Pablo Villoslada
Study Code: MS03

Center: .....
Initials: .....

I (participant name), ...

I have read and understood the information provided.
I have had the opportunity to ask questions.
I have received sufficient information about the study.
I have spoken with (investigator name): .....
I understand that participation is voluntary.
I understand that I am free to withdraw at any time without explanation, without affecting my medical care or rights.
I understand I will not receive any financial benefit from participating.
I freely consent to participate and authorize the use of my data under the conditions described.

Yes ◯
No ◯

I authorize the anonymized use of my data in future scientific research, ensuring confidentiality.

Yes ◯
No ◯

Patient signature	Investigator signature
Name:	Name:
Date:	Date:

This document will be signed in duplicate: one copy for the investigator and one for the patient.