Partners HealthCare System
Research Consent Form

Subject Identification

General Consent Form Template
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Protocol Title: TENS Therapy for Neuropathic Pain in NMOSD

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Description of Subject Population: Neuromyelitis Optica Spectrum Disorder

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Partners now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

This research is being done to evaluate the tolerability and effectiveness of a technique called Quell Flex TENS Therapy (Quell Flex) for the treatment of persistent central neuropathic pain in patients with neuromyelitis optica spectrum disorder (NMOSD). We also plan to study the feasibility of conducting a larger study, and the effect of Quell Flex therapy on quality of life.

NMOSD is an autoimmune disease of the central nervous system that causes recurrent attacks to the spinal cord and optic nerves. Because of spinal cord damage, patients have reported that pain is among the most prevalent and debilitating symptoms, affecting 62-91%. The most frequently-used medications for the treatment of neuropathic pain from any cause are anti-epileptic, antidepressant, opioid and non-steroidal anti-inflammatory agents. We want to find out what effects (good and bad) people experiencing central neuropathic pain get when they undergo Quell Flex therapy in addition to the standard of care for treatment. To assess the effect, participants will receive study technique or sham. Sham is a faked intervention that is not thought to be therapeutically necessary or beneficial, but is an important part of scientific control.

The use of Quell Flex Therapy is approved for marketing by the Food and Drug Administration (FDA) for chronic pain like you have, but has not specifically been studied in patients with NMOSD.

In this consent form, the term "study procedure" refers to both Quell Flex procedure and sham.

People with NMOSD may join.

How many people will be in this study?

About 46 people are expected to take part in this study.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 16 weeks to complete the study. During this time, we will ask you to make zero (0) study visits to Mass General. The entirely of the study is being conducted remotely.

What will happen if you take part in this research study?

If you agree to be in this study, we will ask you to do the following things:

Prior to initiation of Quell Flex Therapy or sham, you will be asked to rate your pain and complete a questionnaire to assess quality of life. You will be randomly assigned to receive one of multiple treatments for 4 consecutive weeks or sham. Random assignment refers to the use of chance procedures to ensure that each participant has the same opportunity to be assigned to any given group, like flipping a coin. Neither you nor our study team will know if you received an actual or a sham device until the study is complete.

You will be screened to see if you are eligible to take part in the study. We will review your MRI and clinical records. If the screening confirms you can be in the study, you will continue to the initial experimental phase of the study. At this point, we will ship you a Quell Flex device.

At enrollment, you will be instructed on how to use the device. We will teach you through a Zoom session how to apply the electrodes to your back corresponding to the location of your pain. You will be trained to use the smartphone app to find the appropriate settings for your device. We will increase the intensity of the stimulation until it is the highest you can tolerate without being painful. We are testing different protocols – some of them can be felt on the skin or underlying muscles while some of them cannot.

You will be asked to rate your pain prior to starting the trial, and every week thereafter. The procedure will continue for at least an hour, and preferably three hours per day for 4 weeks. You will be asked to again complete a questionnaire and rate your pain after the full 4-week course of TENS or sham has been administered. The questionnaire will be conducted via a Zoom call with the study coordinator.

After four weeks, all participants will be rolled over to the open label phase. Each person will receive a new device. You may or may not notice the sensations from this new device, and it may not feel the same as your initial treatment. Again during this phase, we will ask you to rate your pain scores each week and complete a questionnaire at the end of this open label period, which will also last 4 weeks. Four and eight weeks after the conclusion of this phase, we will contact you to assess pain levels.

You may continue all pain medications for the duration of the study, as prescribed by your primary health care provider/neurologist.

Each participant will be offered a standard Quell Flex unit to keep after the study is complete.

Why might you choose to take part in this study?

We cannot promise any benefits to you from taking part in this research study. However, possible benefits may include reduction of pain. Others with neuromyelitis optica spectrum disorder may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include discomfort associated with the Quell Flex device or a rash from the gel on the electrodes.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?" Another thing to consider is the time commitment required to participate in this study. Please note that you can continue your daily activities while wearing the Quell Flex device.

What other treatments or procedures are available for your condition?

Other treatments or procedures that are available for pain include other TENS units available at your local pharmacy, medications, exercise and other non-medical interventions.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Michael Levy, MD, PhD is the person in charge of this research study. You can call him at 410-979-8297 at any time of any day for an emergency. If you have questions about the research study, the scheduling of appointments or study visits, or about the operation of the device, call Gabriela Romanow at 617-784-2598.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

How may we use and share your samples and health information for other research?

The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

- Generally, we will not give you or your doctor information about the results of your individual participation in the research study, though we will share the overall study results with you. The research we are doing is only a steppingstone in understanding pain in NMOSD. Most of the findings that come from studying your samples or information will not be relevant to your personal health. However, in the future, this may change.
- It is important to remember that research results are not always meaningful and are not the same as clinical tests.
- At the conclusion of the first month, we will send a new Quell Flex TENS device to use in the second month of the trial. At the conclusion of the entire trial, we will inform you if you were randomized to the treatment group or the sham group. If you so desire, at the end of the study, you may keep a working device.
- We will publish what we learn in medical journals.

What are the risks and possible discomforts from being in this research study?

The Quell Flex TENS device is FDA-cleared for over-the-counter sale for management of chronic intractable pain.

Skin irritation is a rare side effect but could occur during treatment from the electrodes or gel that is used. It is possible that the device will worsen neuropathic pain.

What other treatments or procedures are available for your condition?

Central neuropathic pain in NMOSD is very common. Despite the high frequency of neuropathic pain in NMOSD, there are no approved treatment options and no standard of care for workup or treatment.

At the Mass General NMO Clinic, we employ several treatment options that can be used in parallel. Importantly, none of the approaches work for all patients. These are used on a trial-and-error basis where successful approaches are maintained while unsuccessful ones are discarded.

The specific treatment approaches we use for neuropathic pain in NMOSD are:

1. Medications:
    a. Anti-epileptic medications such as gabapentin, pregabalin, carbamazepine and oxcarbazepine
    b. Anti-depressant medications including duloxetine and amitriptyline
    c. Anti-spasmodics including baclofen and tizanidine
    d. Pain medications including tramadol
2. Exercise:
    a. Physical therapy
    b. Aquatherapy
    c. Stretching
    d. Yoga
3. Psychological
    a. Biofeedback
    b. Cognitive behavioral therapy
4. Alternatives/Experimental
    a. Acupuncture
    b. Transcutaneous electrical nerve stimulators
    c. Spinal stimulators

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

There is no cost to you to participate in this study. We will cover costs associated with the device and shipping. You will be able to keep the device for your continued use after the study if you so desire. Costs that you may incur that will not be covered are:

1. Electricity costs to charge the device (approximately $2/year)
2. Data costs to use your smartphone for this study (rates vary depending on your cell provider)

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study

- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other: N/A

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____ _____ _____

Subject Date Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent Date Time (optional)

Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

The consent form was presented orally to the subject in the subject's own language, the subject was given the opportunity to ask questions, and the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

Making his/her mark above

Other means _____
(fill in above)

Consent Form Version: 1.0