Consent Form B: Consent for Participation in a Research Study Phase II

Protocol Title: The Effect of Treatment with the PathMaker MyoRegulator™ System Incorporating Trans-spinal Direct Current Stimulation in Patients with Severe Hand Spasticity After Stroke

Principal Investigator: Bruce T. Volpe, MD
Sponsor: None (Investigator Initiated with device provided by PathMaker Neurosystems, Inc.)

This consent form is written from the point of view of a research subject. If consent will be obtained from a legally authorized representative or next of kin, the words "you" and "your" should be read as "the research subject."

As the subject's legally authorized representative or next of kin, you are being asked to give consent for the subject to be in a research study. You are being asked to do this because the subject is not able to give consent. When making this decision you should take into account the wishes of the subject. If you agree to allow the subject to take part in this research, the subject will also be asked to give consent, but only if he/she regains the ability to make healthcare decisions.

Introduction
You are being asked to join a research study. The purpose of a research study is to answer specific questions, sometimes about the safety of a drug or device and how well it works. Being in a research study is different from being a patient. When you are a patient, you and your doctor have freedom in making decisions about your healthcare. When you are in a research study, the researcher will follow the rules of the research study as closely as possible, while monitoring your health.

This consent form will explain:

- the purpose of the study
- what you will be asked to do
- the potential risks and benefits

It will also explain that you do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why is this research study being done?
The goal of this research study is to better understand and improve the treatment muscle spasticity (e.g. muscle tightness) after stroke with the hope of maximizing this recovery. Specifically, we wish to examine if multiple sessions of non-invasive peripheral nerve and spinal cord stimulation with an investigational device called the MyoRegulator™, can reduce muscle tightness of the wrist and hand and improve hand function.

You are being asked to participate because you have had a stroke with resulting muscle spasticity of the wrist and hand.

How many people will take part in this study?
We hope to enroll a total of 30 post-stroke participants in this study.

How long will you be in this study?
If you choose to participate in this research study, the duration of participation will be up to 10 weeks. During this time, there will be 15-20 study visits, up to 90 minutes each. These study visits will take place at the Feinstein Institute for Medical Research (350 Community Drive, Manhasset, NY).

What will happen in this research study?
There are several procedures that you will be asked to complete during the study visits and are described below**:**

Screening questionnaire
You will be asked to complete a questionnaire about your health history to see if you have any risk factors that would prevent you from undergoing spinal stimulation. This will take only a few minutes

Clinical measures
You will complete a series of evaluations to assess the strength and function of your muscles. This will take approximately 45 minutes.

Audiovisual Recordings (Optional)
You may be asked to have photos and video recordings taken during clinical measures. These photos and videos would be designed to document your improvement, and to share potential improvements with the device manufacturer, Pathmaker Neurosystems. These photos videos may be used in promotional demonstrations to the public. Photo and video recording is optional. You may still participate in this study if you refuse to be recorded. If you do agree to be recorded, you will sign a photo and video release.

Do you agree to have photos/videos of you taken during this study?

□ Yes, I agree to photos/videos taken of me during the study.

□ No, I do not agree to photos/videos taken of me during the study.

Instrumental assessment
You will be seated in a chair and hold onto a joystick while resting your forearm in a trough. A motor will gently bend and flex your wrist and measure the amount of muscle tone during the movement. Additionally, a set of surface EMG electrodes will be placed on your wrist and hand to measure these movements. This will take approximately 15 minutes.

Peripheral Nerve and Spinal Cord Stimulation

The MyoRegulator™: This device pairs trans-spinal direct current stimulation (tsDCS) with peripheral DC stimulation (pDCS), to alter the spasticity in the affected upper extremity of patients with stroke. The MyoRegulator™ is not currently approved by the FDA, and is considered investigational for the purposes of this study. However, tsDCS has been successfully used in several human and animal research studies to change muscle tone/stiffness and change muscle reflex responses, suggesting a potential therapeutic benefit to patients with hand spasticity (muscle tightness) after stroke.

In this study, you will be seated in a chair during stimulation sessions, and two sets of two electrodes will be positioned on your wrist, neck, and stomach. The first electrode will be placed on the base of the neck with its pair placed at the base of the abdomen, just above the hip. The second set of electrodes will be placed on the wrist and forearm. The electrodes will be connected to a battery-driven stimulator. A small electrical current will be applied to your spinal cord and wrist for 20 minutes.

You will receive a total of 10 sessions of combined trans-spinal and peripheral nerve stimulation. In one half of the sessions, the current will be turned on (active stimulation), and in the other half of the sessions the current will be turned off ("sham" stimulation). Sham stimulation has no actual electric current. It is compared to stimulation with electric current to see if the stimulation has a real effect. You will not be told which sessions will be real and which will be sham. This is called blinding, and is a process used to prevent the subject from knowing which group s/he is in. It is used to make sure the study data will not be biased. You will be asked at two time-points in the study which type of stimulation (sham or active) you believe you received. In case of emergency, the investigators can inform you of which stimulation you are receiving.

Schedule of Visits
The schedule of study visits is below and describes what procedures will be done at each study visit:

Lead-in Period

- Week 1, Visit 1 (approximately 90 minutes)
    - Baseline clinical outcome measures
    - Instrumental measures with EMG
    - Medical screening
    - Consent
- Week 1, Visits 2-3 (approximately 60 minutes each)
    - Baseline clinical outcome measures
    - Instrumental measures with EMG

Training Period Phase I

- Week 2, Visit 4-7 (approximately 60 minutes)
    - 20 min of peripheral nerve and spinal stimulation (pDCS+tsDCS) condition 1 (real or sham)
    - Instrumental measures with EMG before and 10 minutes post-stimulation

    - Clinical measures during 1-2 visits
- Week 2, Visit 8 (approximately 90 minutes)
    - 20 min of peripheral nerve and spinal stimulation (pDCS+tsDCS) condition 1 (real or sham)
    - Instrumental measures with EMG before and 10 minutes post-stimulation
    - Clinical measures

Follow Up Testing Phase I

- Week 3, Visit 9 (approximately 60 minutes)
    - Clinical follow-up measures
    - Instrumental measures with EMG

Training Period Phase II

- Week 4, Visit 10-13 (approximately 60 minutes)
    - 20 min of peripheral nerve and spinal stimulation (pDCS+tsDCS) condition 2 (real or sham)
    - Instrumental measures with EMG before and 10 minutes post-stimulation
    - Clinical measures during 1-2 visits
- Week 4, Visit 14 (approximately 90 minutes)
    - 20 min of peripheral nerve and spinal stimulation (pDCS+tsDCS) condition 2 (real or sham)
    - Instrumental measures with EMG before and 10 minutes post-stimulation
    - Clinical discharge measures

Follow Up Testing Phase II

- Week 5-10, Visit 15-20 (approximately 60 minutes)
    - Clinical follow-up measures
      Instrumental measures with EMG

Participation in this study also allows investigators access to your medical records. They will record your age, gender, and date of stroke/results of the medical imaging you had done following the stroke.

What are the risks of the research study? What could go wrong?
pDCS and tsDCS have the potential to cause redness of the skin around the area of the electrode pads. Such reddening has been found to go away quickly after the stimulation ends for most study participants, however there is a small risk of more significant redness and soreness similar to a sunburn. If you think it is needed, we can apply a cold compress over the red area. There may be a tolerable sensation of pins and needles under the electrode pads. This sensation is not usually considered painful, but some people might find it uncomfortable. If you have a loop recorder, there is a small risk of disruption to the cardiac monitoring data. However, your Cardiologist has been made aware of this risk and has cleared you for the study. There is a small additional risk of over-activating the nerve at the wrist. However, stimulation intensity at both the wrist muscle and nerve will be continuously monitored with EMG to ensure that stimulation

level remains subthreshold.This means that the levels of stimulation will remain well below the level of activation, and remain without risk of over-activation.

There may be risks that are unknown at this time.

What are the benefits of this research study?
We cannot predict whether you will experience direct benefits from the stimulation. However, knowledge may be gained which may benefit patients with stroke in the future.

If you do not want to take part in this research study, what are your other choices?
If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices. Your other choices may include:

- Standard treatment

Your doctor can also tell you the important risks and benefits associated with the alternative treatment.

Are there any costs for being in this research study?
You will not incur any additional costs associated with this study. All study-related procedures and medications will be provided at no cost to you. Costs related to standard medical practice will be billed as usual to you or your insurance carrier.

Will you receive any payments for participating in this research study?
Parking during your study participation will be provided on site at no cost to you. You will not be paid for participating in this study.

If the research produces marketable products, will you receive any payment?
If this research produces a marketable product, there are no plans for you to receive any money.

What happens if you are injured while participating in this study? If you are hurt from being in the study, you will receive medical care and treatment as needed from Northwell Health. PathMaker Neurosystems Inc. will be responsible for any damages/injuries that may occur as a result of material malfunction of the MyoRegulator device. Otherwise, you will be responsible for the costs of such medical treatment, directly or through your medical insurance and/or other forms of medical coverage. No money will be given to you.

What are your rights as a research participant?
Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study, you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at Northwell Health. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by an investigator or the IRB. Reasons for withdrawal may include:

- failure to show up for study visits,
- it is not in your best interests to continue on this study
- the study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data (or samples) already collected will continue to be used. However, no new information will be collected.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What information will be collected and used for this study?
If you agree to be in this study, we will collect health information that identifies you. We may collect the results of tests and interviews. We may also collect information from your medical record. We will only collect information that is needed for research. Such information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization. If you do not want to provide authorization, then you cannot participate in this research study.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health, except at detailed below.

- Investigators may share the results of your study tests and procedures with your doctor or clinical staff not involved in the study, but who may be involved in your treatment.

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from federal and state government oversight agencies such as the National Institutes of Health (NIH) and/or the Food and Drug Administration (FDA),
- Representatives from the Northwell Health Human Research Protection Program (the group of people that oversee research at this institution)

The data from this study may also be used to support regulatory approvals of the pDCS + tsDCS device used in the study. This means that your health information and test data related to this study may be disclosed to the device manufacturer, PathMaker Neurosystems, Inc., and to regulatory agencies including the US Food and Drug Administration as well as regulatory agencies in other countries. However, data disclosed for this purpose will not identify you by name, address, telephone number or any other personal identifier; only a patient ID code will be used.

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it will be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, please call the Human Research Protection Program at 516-321-2100.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?
If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Bruce T. Volpe, MD
Feinstein Institute for Medical Research
350 Community Drive
Manhasset, NY 11030

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those individuals who stay in it.

Will information about this study be available to the public?
A description of this clinical trial will be available on http://www.Clinical Trials.gov , as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Does the investigator of this study receive money if you take part?
The investigators on this study do not receive money for your participation in this study.

Who can answer your questions about this study?
If you have any questions about the study, or about side effects or injury caused by research, call Bruce T. Volpe, MD at (516) 562-3384. If you need emergency care go to the nearest Emergency Department or dial 911. If you have questions about your rights as a research subject you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 321-2100. A signed copy of this consent form will be given to you.

SUMMATION & SIGNATURES: You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

SIGNATURE PAGE TO FOLLOW

Please sign as "subject" if you agree to participate in the study and have the capacity to self-consent:

Subject's Printed Name	Subject's Signature	Date

Witness's Printed Name	Witness's Signature	Date

Investigator's Statement: In addition to advising the above subject about the research study, I have offered an opportunity for further explanation of the risks and discomfort which are, or may be associated with this study and to answer any further questions relating to it.

Investigator's Printed Name	
Investigator's Signature	Date

OR

Please sign as the designated "Legally Authorized Representative" on behalf of the participant, if the participant has the capacity to self-consent, but was unable to sign due to a physical disability (e.g. hand weakness, visual deficits):

_____	_____
Subject's Printed Name	Date

_____	_____	_____
Legally Authorized Representative's or Next-of-Kin Printed Name	Legally Authorized Representative's or Next-of-Kin Signature	Date

Witness' Statement: I was present during the consent process of the above mentioned research study. A member of the research team explained the research study entirely and allowed ample opportunity for the subject to ask any questions or express any concerns. The subject was unable to sign the consent form due to a physical disability, however, voluntarily agreed to participate in the research study by providing verbal assent. By signing below, I attest to this statement.

_____	_____	_____
Witness Printed Name	Witness Signature	Date

Investigator's Statement: In addition to advising the above subject about the research study, I have offered an opportunity for further explanation of the risks and discomfort which are, or may be associated with this study and to answer any further questions relating to it.

_____	
Investigator's Printed Name	
_____	_____
Investigator's Signature	Date

OR

Please sign as the designated "Legally Authorized Representative" on behalf of the participant, if the participant does not have the capacity to self-consent:

_____	_____	_____
Legally Authorized Representative's or Next-of-Kin Printed Name	Legally Authorized Representative's or Next-of-Kin Signature	Date

Description of signer's authority to act on behalf of the subject:

_____

_____	_____	_____
Witness's Printed Name	Witness's Signature	Date

☐ Witness signature waived (signed consent emailed, faxed, or mailed to investigator)

Investigator's Statement: In addition to advising the above subject about the research study, I have offered an opportunity for further explanation of the risks and discomfort which are, or may be associated with this study and to answer any further questions relating to it.

_____
Investigator's Printed Name

_____	_____
Investigator's Signature	Date

**If you have signed the above consent as the legally authorized representative (LAR), please attempt to have the study participant sign this assent, in order to include him/her in his/her consent process:*

ASSENT BY ADULT SUBJECT WITH A LEGALLY AUTHORIZED REPRESENTATIVE

I have been asked to join this research study. I have the right to find out what will or might happen to me if I am in the study. I have the right to tell the doctor, and the person legally allowed to make decisions for me, that I do or do not want to participate.

The person legally allowed to make decisions for me will also be asked to give permission for me to join this study.

(Investigator's name)_____ and _____, the person legally allowed to make decisions for me, have explained what I will have to do in the study.

(Investigator's name)_____ and _____, the person legally allowed to make decisions for me, have explained the discomforts, risks and inconveniences I may have if I join the study.

I have asked any questions I had, and all my questions have been answered.

_____ I agree to be in this study.

_____ I do not want to be in this study.

_____
Subject's name

_____ _____
Put your name here ↑ Date

_____ _____ _____
Witness's Printed Name Witness's Signature Date

All procedures, risks and discomforts have been explained to the subject.

_____
Investigator's printed name

_____ _____
Investigator's Signature Date

**If you have signed the consent as the legally authorized representative (LAR), and during the study the participant regains the capacity to self-consent, please have him/her sign as "subject":*

Addendum to Consent by Research Proxyfor Continuing Participation in a Research Study
Protocol Title: The Effect of Treatment with the PathMaker MyoRegulator™ System Incorporating Trans-spinal Direct Current Stimulation in Patients with Severe Hand Spasticity After Stroke
Principal Investigator: Bruce T. Volpe, MD
Sponsor: None (Investigator-Initiated)

- I have been told that my research proxy gave consent for me to be in the above titled research study.
- I am now able to give my own consent to be in the research study.
- I have been told of the purpose of the research, what my participation will entail, as well as all of the potential risks and benefits.
- I have discussed the research study with the study doctor and have received satisfactory answers to any questions.
- I have been told that I may ask more questions at any time.
- I do not have to stay in this research study. My decision to continue is completely voluntary. If I wish to leave the study, I may have to undergo final follow-up tests to assure my well-being. If I leave the study I will not suffer any penalty or loss of benefits to which I am entitled.
- I have been told that all of the elements of informed consent in the attached consent form, signed by my research proxy, are still applicable.
- I have reviewed the consent document and have discussed all of the elements of informed consent with the study doctor. I agree to stay in the above titled research study.

_____ _____
Signature of Subject Date

_____
Printed Name of Subject

_____ _____
Witness Signature Date

_____
Printed Name of Witness

In addition to advising the above subject about the research study, I have offered an opportunity for further explanation of the risks and discomfort which are, or may be associated with this study and to answer any further questions relating to it.

_____ _____
Investigator's Signature Date